Proposed Decision Memo for Computed Tomographic Angiography (CAG-00385N)

Decision Summary

The Centers for Medicare and Medicaid Services (CMS) proposes the following be added to section 220.1 (Appendix A) of the National Coverage Determination Manual titled “Computed Tomography”:

The evidence is inadequate to conclude that cardiac computed tomographic angiography (CTA) is reasonable and necessary under section 1862(a)(1)(A) for the diagnosis of coronary artery disease (CAD); however, the agency believes the evidence is promising for two clinical indications and that coverage with evidence development (CED) would be appropriate for these indications under section 1862(a)(1)(E), based on the specific standards outlined below.

Therefore, CMS proposes Medicare coverage of CTA for the diagnosis of CAD for:

- symptomatic patients with chronic stable angina at intermediate risk of CAD; or
- symptomatic patients with unstable angina at a low risk of short-term death and intermediate risk of CAD.

Risk of CAD is determined by the Framingham risk score (FRS). Patients with FRS >20% are considered high risk; FRS of 10%-20% are considered intermediate risk (Keevil, 2007; Wilson, 1998).

A clinical study seeking Medicare payment for CTA for the diagnosis of CAD for the above clinical indications provided to the beneficiary pursuant to CED must address one or more of the following questions:

- Does cardiac CTA have the ability to diagnose or exclude coronary artery disease as well as invasive coronary angiography?
- Does coronary CTA reduce the need for invasive coronary angiography?
- Does coronary CTA improve health outcomes for patients with acute chest pain who present in the emergency room or other setting?

CMS is requiring that the study meet the following standards:

- The principal purpose of the research study is to test whether the intervention potentially improves the participants' health outcomes;
- The research study is well-supported by available scientific and medical information or it is intended to clarify or establish the health outcomes of interventions already in common clinical use;
- The research study does not unjustifiably duplicate existing studies;
- The research study design is appropriate to answer the research question being asked in the trial;
- The research study is sponsored by an organization or individual capable of executing the proposed trial successfully;
- The research study is in compliance with Federal regulations concerning the protection of human subjects found at 45 CFR Part 46. If a study is FDA-regulated, it also must be in compliance with 21 CFR Parts 50 and 56;
- All aspects of the research study are conducted according to the appropriate standards of scientific integrity.
- The research study has a written protocol that clearly addresses, or incorporates by reference, the Medicare standards;
- The research study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals. Trials of all medical technologies measuring therapeutic outcomes as one of the objectives meet this standard only if the disease or condition being studied is life-threatening as defined in 21 CFR §312.18(a) and the patient has no other viable treatment options;
- The research study is registered on the ClinicalTrials.gov website by the principal sponsor/investigator prior to the enrollment of the first study subject;
- The research study protocol specifies the method and timing of public release of all prespecified outcomes to be measured including release of outcomes if outcomes are negative or study is terminated early. The results must be made public within 24 months of the end of data collection. If a report is planned to be published in a peer-reviewed journal, then that initial release may be an abstract that meets the requirements of the International Committee of Medical Journal Editors. However, a full report of the outcomes must be made public no later than three years after the end of data collection.

- The research study protocol must explicitly discuss subpopulations affected by the treatment under investigation, particularly traditionally underrepresented groups in clinical studies, how the inclusion and exclusion criteria affect enrollment of these populations, and a plan for the retention and reporting of said populations on the trial. If the inclusion and exclusion criteria are expected to have a negative effect on recruitment or retention of the underrepresented populations, the protocol must discuss why these criteria are necessary; and
- The research study protocol explicitly discusses how the results are or are not expected to be generalizable to the Medicare population to infer whether Medicare patients may benefit from the intervention. Separate discussions in the protocol may be necessary for populations eligible for Medicare due to age, disability or Medicaid eligibility.

The principal investigators of CTA clinical studies seeking Medicare payment should submit the following documentation to CMS and should expect to be notified when the CMS review is complete:

- Complete study protocol;
- Protocol summary;
- Statement that the above study standards are met;
- Statement that the study addresses at least one of the above questions related to CTA;
- Complete contact information (phone number, email address and mailing address); and
- Clinicaltrials.gov registration number.

The above information should be mailed to:

Steve E. Phurrough, MD, MPA
Director
Coverage and Analysis Group, CMS
Re: CTA
Mailstop C1-09-06
7500 Security Blvd.
Baltimore, MD 21244-1850

All other uses of cardiac CTA for the diagnosis of CAD are noncovered. Congress has not established a screening benefit for cardiac CTA for the diagnosis of CAD; thus the use of cardiac CTA to screen asymptomatic patients for CAD is also noncovered.

Cardiac CTA for uses other than the diagnosis of CAD remains at contractor discretion.

We are requesting public comments on this proposed determination pursuant to Section 731 of the Medicare Modernization Act. After considering the public comments, we will make a final determination and issue a final decision memorandum.

Back to Top

Proposed Decision Memo

TO: Administrative File: CAG 00385N
Computer Tomographic Angiography

FROM:

Steve E. Phurrough, MD, MPA
Director, Coverage and Analysis Group

Marcel E. Salive, MD, MPH
Director, Division of Medical and Surgical Services

JoAnna Baldwin, MS
Lead Analyst

Joseph Chin, MD, MS
Lead Medical Officer

SUBJECT: Proposed Coverage Decision Memorandum for Cardiac Computed Tomographic Angiography for the Diagnosis of Coronary Artery Disease

DATE: December 13, 2007

I. Decision

The Centers for Medicare and Medicaid Services (CMS) proposes the following be added to section 220.1 (Appendix A) of the National Coverage Determination Manual titled “Computed Tomography”:

The evidence is inadequate to conclude that cardiac computed tomographic angiography (CTA) is reasonable and necessary under section 1862(a)(1)(A) for the diagnosis of coronary artery disease (CAD); however, the agency believes the evidence is promising for two clinical indications and that coverage with evidence development (CED) would be appropriate for these indications under section 1862(a)(1)(E), based on the specific standards outlined below.

Therefore, CMS proposes Medicare coverage of CTA for the diagnosis of CAD for:

- symptomatic patients with chronic stable angina at intermediate risk of CAD; or
- symptomatic patients with unstable angina at a low risk of short-term death and intermediate risk of CAD.

Risk of CAD is determined by the Framingham risk score (FRS). Patients with FRS >20% are considered high risk; FRS of 10%-20% are considered intermediate risk (Keevil, 2007; Wilson, 1998).

A clinical study seeking Medicare payment for CTA for the diagnosis of CAD for the above clinical indications provided to the beneficiary pursuant to CED must address one or more of the following questions:

- Does cardiac CTA have the ability to diagnose or exclude coronary artery disease as well as invasive coronary angiography?
- Does coronary CTA reduce the need for invasive coronary angiography?
- Does coronary CTA improve health outcomes for patients with acute chest pain who present in the emergency room or other setting?

CMS is requiring that the study meet the following standards:

- The principal purpose of the research study is to test whether the intervention potentially improves the participants' health outcomes;
- The research study is well-supported by available scientific and medical information or it is intended to clarify or establish the health outcomes of interventions already in common clinical use;
- The research study does not unjustifiably duplicate existing studies;
- The research study design is appropriate to answer the research question being asked in the trial;
- The research study is sponsored by an organization or individual capable of executing the proposed trial successfully;
- The research study is in compliance with Federal regulations concerning the protection of human subjects found at 45 CFR Part 46. If a study is FDA-regulated, it also must be in compliance with 21 CFR Parts 50 and 56;
- All aspects of the research study are conducted according to the appropriate standards of scientific integrity.
- The research study has a written protocol that clearly addresses, or incorporates by reference, the Medicare standards;
- The research study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals. Trials of all medical technologies measuring therapeutic outcomes as one of the objectives meet this standard only if the disease or condition being studied is life-threatening as defined in 21 CFR §312.18(a) and the patient has no other viable treatment options;
- The research study is registered on the ClinicalTrials.gov website by the principal sponsor/investigator prior to the enrollment of the first study subject;

- The research study protocol specifies the method and timing of public release of all prespecified outcomes to be measured including release of outcomes if outcomes are negative or study is terminated early. The results must be made public within 24 months of the end of data collection. If a report is planned to be published in a peer-reviewed journal, then that initial release may be an abstract that meets the requirements of the International Committee of Medical Journal Editors. However, a full report of the outcomes must be made public no later than three years after the end of data collection.
- The research study protocol must explicitly discuss subpopulations affected by the treatment under investigation, particularly traditionally underrepresented groups in clinical studies, how the inclusion and exclusion criteria affect enrollment of these populations, and a plan for the retention and reporting of said populations on the trial. If the inclusion and exclusion criteria are expected to have a negative effect on recruitment or retention of the underrepresented populations, the protocol must discuss why these criteria are necessary; and
- The research study protocol explicitly discusses how the results are or are not expected to be generalizable to the Medicare population to infer whether Medicare patients may benefit from the intervention. Separate discussions in the protocol may be necessary for populations eligible for Medicare due to age, disability or Medicaid eligibility.

The principal investigators of CTA clinical studies seeking Medicare payment should submit the following documentation to CMS and should expect to be notified when the CMS review is complete:

- Complete study protocol;
- Protocol summary;
- Statement that the above study standards are met;
- Statement that the study addresses at least one of the above questions related to CTA;
- Complete contact information (phone number, email address and mailing address); and
- Clinicaltrials.gov registration number.

The above information should be mailed to:

Steve E. Phurrough, MD, MPA
Director
Coverage and Analysis Group, CMS
Re: CTA
Mailstop C1-09-06
7500 Security Blvd.
Baltimore, MD 21244-1850

All other uses of cardiac CTA for the diagnosis of CAD are noncovered. Congress has not established a screening benefit for cardiac CTA for the diagnosis of CAD; thus the use of cardiac CTA to screen asymptomatic patients for CAD is also noncovered.

Cardiac CTA for uses other than the diagnosis of CAD remains at contractor discretion.

We are requesting public comments on this proposed determination pursuant to Section 731 of the Medicare Modernization Act. After considering the public comments, we will make a final determination and issue a final decision memorandum.

II. Background

Computed tomographic angiography (CTA) is a general phrase used to describe noninvasive imaging of the arteries with various types of computed tomography (CT) machines, such as multislice CT (MSCT), multidetector CT (MDCT), and dual source CT (DSCT).

The use of CTA has increased over the years due to advances in the technology and rapid diffusion of the machines outside the hospital settings. The initial single slice CT machines produced poor quality images. In the late 1990's, 4 slice CT machines were introduced, with 16 slice and 64 slice CT machines following shortly afterwards. Image quality and performance reportedly increased with each model. However, questions remain on the indications for use.

A particular focus has been the use of CTA for evaluation of the coronary arteries in patients with chest pain. Proponents have claimed that cardiac or coronary CTA may reduce the need for invasive coronary angiography for certain patients. Critics have pointed out the lack of evidence on outcomes and the limitations to the technology including uninterpretable/unassessable segments and the health risks from the considerable radiation exposure. Although there are other uses of CTA, this decision focuses only on the use of CTA for the evaluation of the coronary arteries in patients with symptomatic coronary artery disease (e.g., chest pain). Imaging performed on patients without chest pain (asymptomatic patients) would be considered screening and is not an available benefit in the Medicare program.

Chest pain (angina pectoris) can be classified as “typical angina, atypical angina and noncardiac chest pain” (Snow, 2004 – Appendix C). Angina is defined “as a clinical syndrome characterized by discomfort in the chest, jaw, shoulder, back, or arm” (Snow, 2004). Unstable angina is defined as “angina that presents in 1 of 3 principal ways: rest angina, severe new-onset angina, or increasing angina” (Snow, 2004).

Given the prevalence and incidence of CAD in the US, angina has been well studied and evidence-based guidelines are available for unstable and stable angina. The ACC/AHA guidelines on unstable angina (Gibbons, 2007) and chronic stable angina (Gibbons, 2002) are such examples and are well recognized and accepted. Although these guidelines do not directly incorporate coronary CTA, the treatment algorithms provide clues on possible scenarios where CTA may be considered.

For unstable angina, patients who are at high or intermediate short term risk of death (Appendix C) are almost always treated as inpatients in the hospital setting. These patients typically undergo cardiac catheterization and invasive coronary angiography so the role of CTA is very limited (Anderson, 2007). However, “low-risk patients with unstable angina have a short-term risk not substantially different from those with stable angina” and “their evaluation can be accomplished safely and expeditiously in an outpatient setting” (Gibbons, 2002).

For chronic stable angina, the ACC/AHA and ACP have developed guidelines with treatment algorithms that may also help guide the consideration for use of imaging such as coronary CTA (Gibbons, 2002). Specifically, for patients with chronic stable angina and an intermediate risk of CAD, imaging may be considered when the exercise test does not suggest high risk and there is inadequate information on diagnosis (Appendix C). The risk of CAD may be determined by several methods. The most commonly used and accepted is the Framingham Risk Score (Appendix C). Patients with FRS >20% are considered high risk; FRS of 10%-20% are considered intermediate risk (Keevil, 2007; Wilson, 1998). Exercise stress testing also provides a measure of risk through the Duke treadmill score (Gibbons, 2002).

Appropriateness criteria have also been published (Hendel, 2006). While these were based on consensus, the criteria may provide additional information on specific uses of CTA, especially for those indications which were considered inappropriate. Most studies, as noted in the Blue Cross Blue Shield technology assessments, have not specifically evaluated long term health outcomes but have looked at diagnostic test characteristics and test performance compared to invasive angiography. The question of how coronary CTA may fit into the current recommended clinical pathways needs to be addressed by research and clinical experts.

In addition, there are a number of aspects or dimensions of imaging quality, as noted by Douglas and colleagues (Douglas et al., 2006), that are relevant and applicable to coronary CTA. Many of these aspects are implicit in the process of imaging but being such may be areas that deserve some explicit focus to ensure that quality is maintained and not forgotten in everyday practice.

III. History of Medicare Coverage

Medicare has an NCD, last revised in 1985, that discusses general uses of CT. The policy does not specifically address the use of CTA technology or CT for the diagnosis of CAD as such an indication was not in clinical practice at the time the policy was last updated. Therefore, CTA has never been addressed through national policy and in the absence of national policy that addresses CTA, coverage is at the discretion of local Medicare contractors. The majority of local contractors have similar local coverage determination policies (LCDs) on CTA.

Medicare is a defined benefit program (§ 1812 (Scope of Part A); § 1832 (Scope of Part B) § 1861(s) (Definition of Medical and Other Health Services)). An item or service must fall within a benefit category as a prerequisite to Medicare coverage. CTA may be eligible for coverage under the Social Security Act section 1861(s)(3) “diagnostic X-ray tests”.

IV. Timeline of Recent Activities

June 13, 2007	CMS opens National Coverage Analysis for CTA.
July 13, 2007	Initial 30-day public comment period ends.

V. FDA Status

Currently, CT imaging systems and post-processing software go through the 510(k) process at the FDA to obtain clearance for commercial distribution. To obtain 510(k) clearance, the sponsor must demonstrate that the device is substantially equivalent to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). Below are examples of two CT related devices (one CT scanner and one software system) cleared by the FDA through the 510(k) process. The indications for use were copied from the FDA's 510(k) online database at http://www.fda.gov/cdrh/pdf7/K071806.pdf and http://www.fda.gov/cdrh/pdf6/K062386.pdf respectively.

Device Name: ECLOS Computed Tomography X-ray System
Clearance Dated: August 28, 2007
The ECLOS Computed Tomography system is an x-ray imaging device that produces cross-sectional images of the body at different angles. The system reconstructs, processes, displays, and stores the collected images. The device output can provide an aid to diagnosis when used by a qualified physician and is intended for general purpose CT applications.

Device Name: QAngio CT
Clearance Dated: October 5, 2006
QAngio CT software solution has been developed for the objective and reproducible analysis of vessels in CTA images. It enables the quantitative analysis of CT angiograms based on automated segmentation. More specifically, QAngio CT can be used to quantify a number of lesion characteristics. QAngio CT is intended for use as an auxiliary tool in assessing CTA studies in clinical practice and in clinical trials. The analysis results obtained with QAngio CT are to be interpreted by cardiologists and radiologists.

VI. General Methodological Principles

When making national coverage decisions, CMS evaluates relevant clinical evidence to determine whether or not the evidence is of sufficient quality to support a finding that an item or service falling within a benefit category is reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. The critical appraisal of the evidence enables us to determine to what degree we are confident that: 1) the specific assessment questions can be answered conclusively; and 2) the intervention will improve health outcomes for patients. An improved health outcome is one of several considerations in determining whether an item or service is reasonable and necessary.

A detailed account of the methodological principles of study design that the agency utilizes to assess the relevant literature on a therapeutic or diagnostic item or service for specific conditions can be found in Appendix B. In general, features or clinical studies that improve quality and decrease bias include the selection of a clinically relevant cohort, the consistent use of a single good reference standard, and the blinding of readers of the index test, and reference test results.

Public comments sometimes cite the published clinical evidence and give CMS useful information. Public comments that give information on unpublished evidence such as the results of individual practitioners or patients are less rigorous and therefore less useful for making a coverage determination. Public comments that contain personal health information will not be made available to the public. CMS uses the initial public comments to inform its proposed decision. CMS responds in detail to the public comments on a proposed decision when issuing the final decision memorandum.

VII. Evidence

A. Introduction

In this coverage analysis, we considered coronary CTA studies and evidence that were published after the BCBS TEC assessments (published in 2005 and 2006), since the indications are similar. Most studies have focused on test characteristics and have not considered health outcomes, such as mortality, morbidity or reduction of invasive angiography. We believe that health outcomes are more important than test characteristics. In evaluating diagnostic tests, Mol and colleagues (2003) reported: “Whether or not patients are better off from undergoing a diagnostic test will depend on how test information is used to guide subsequent decisions on starting, stopping, or modifying treatment. Consequently, the practical value of a diagnostic test can only be assessed by taking into account subsequent health outcomes.” When a proven, well established association or pathway is available, intermediate health outcomes may also be considered. For example, if a particular diagnostic test result can be shown to change patient management and other evidence has demonstrated that those patient management changes improve health outcomes, then those separate sources of evidence may be sufficient to demonstrate positive health outcomes from the diagnostic test.

1. Literature Search

CMS searched PubMed from 2005 to present. General keywords included computed tomographic angiography, CTA and coronary. Initially, we searched for studies that presented original data, examined health outcomes and were published in peer-reviewed English language journals. Since only one study met these criteria, the search was expanded to included technology assessments, meta-analysis, reviews, and studies that reported only test characteristics compared to invasive coronary angiography. Abstracts were excluded.

B. Discussion of evidence reviewed

1. Evidence Questions

- Is the evidence sufficient to conclude that cardiac CTA has the ability to diagnosis or exclude coronary artery disease as well as invasive coronary angiography?
- Is the evidence sufficient to conclude that coronary CTA reduces the need for invasive coronary angiography?
- Is the evidence sufficient to conclude that the use of coronary CTA improves health outcomes for patients with acute chest pain who present in the emergency room or other settings?

2. External technology assessments

DHHS Agency for Healthcare Research and Quality. Non-Invasive Imaging for Coronary Artery Disease. AHRQ 2006; available at: http://www.cms.hhs.gov/determinationprocess/downloads/id34TA.pdf [PDF, 251KB].

In 2006, the Agency for Healthcare Research and Quality commissioned a technology assessment on non-invasive imaging for CAD that was performed by Matchar and colleagues at the Duke Evidence-based Practice Center. For CTA, the authors of the assessment noted: "We identified 29 studies using 16-array or greater multi-detector computed tomography (MDCT) assessing coronary CTA for evaluation of native coronary arteries stenosis, and 13 MRA studies evaluating native coronary artery stenosis using more recent MRI imaging sequences. These studies were generally small, performed at single centers, and often did not include information that would serve to provide confident assessments of the key questions. In particular, we did not identify any studies evaluating the clinical impact of diagnostic strategies including NITs [non-invasive imaging tests] of coronary anatomy compared with strategies that did not include these techniques. The populations studied tended to be relatively young (<65 years of age), and limited results subgrouped by age were available."

They concluded: "At present, there is limited evidence regarding test performance of NITs for identifying, quantifying, or otherwise characterizing coronary artery stenoses. The available evidence provides preliminary data on the ability of coronary MRA (1.5 T) and coronary CTA using at least 16-array MDCT technology to detect obstructive coronary artery lesion in the proximal to mid coronary arteries. The evidence regarding detection of coronary lesions in branch vessels or distal coronary arteries remains unclear and may well improve as the technology improves. Studies conducted to date primarily fall into the "proof of concept" category with study patients having a high pre-test probability of CAD. Patients providing suboptimal images were often excluded from calculations of test accuracy. Future work will need to examine these tests in larger, less selected populations representing the clinical settings in which they are actually expected to be used. The effect of biases in selection of study patients and in the publication of accuracy results for these tests was not assessed in this preliminary analysis."

Blue Cross Blue Shield Technology Evaluation Center. Contrast-enhanced cardiac computed tomographic angiography in the diagnosis of coronary artery stenosis or for evaluation of acute chest pain. TEC Assessment Program, Volume 20, No. 4, May 2005.

In 2005, the BCBS TEC published a technology assessment “to evaluate the clinical effectiveness of contrast-enhanced cardiac computed tomographic angiography, hereafter referred to as CTA, for coronary artery evaluation.” Study inclusion criteria were (quoted as follows):
■ Used contrast-enhanced EBCT with slice thickness no greater than 1.5 mm or contrast-enhanced MDCT with at least 16 rows
■ Applied an appropriate reference standard such as conventional coronary angiography or clinical reference standard
■ Reported sensitivity and/or specificity of CTA or sufficient data to generate a 2 × 2 contingency table
■ Included only human subjects
■ Published in English as a full-length, peer-reviewed journal article

Twenty-one studies (16 on MDCT, 6 on EBCT; 1016 total patients) were included in the assessment. The TEC reported:” The evidence is insufficient to determine whether the use of CTA improves net health outcome or whether it is as beneficial as any established alternatives.”
The TEC criteria and results were as follows:
1. The technology must have final approval from the appropriate governmental bodies. (Met)
2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes. (Not met)
3. The technology must improve the net health outcome. (Not met)
4. The technology must be as beneficial as any established alternatives. (Not met)
5. The improvement must be attainable outside the investigational settings. (Not met)

They concluded that: “the use of contrast-enhanced cardiac CT angiography for screening or diagnostic evaluation of the coronary arteries does not meet the TEC criteria.”

Blue Cross Blue Shield Technology Evaluation Center. Contrast-enhanced cardiac computed tomographic angiography in the diagnosis of coronary artery stenosis or for evaluation of acute chest pain. TEC Assessment Program, Volume 21, No. 5, August 2006.

In 2006, the BCBS TEC published an update of their 2005 assessment of CTA. The objective was “to determine the usefulness of CTA as a substitute for coronary angiography for two indications: 1) in the diagnosis of coronary artery stenosis, and 2) in the evaluation of acute chest pain in the emergency room (ER).” The TEC report focused on “studies examining 64-row CTA, which provides better resolution than the previous generation of 16-row machines.” For CTA as a substitute for invasive angiography, study inclusion criteria were (quoted as follows):

- Used contrast-enhanced EBCT with slice thickness no greater than 1.5 mm or contrast-enhanced MDCT with at least 32 rows
- Applied the reference standard of invasive angiography to all patients
- Reported sensitivity and/or specificity of CTA or sufficient data to generate a 2×2 contingency table
- Included only human subjects
- Published in English as a full-length, peer-reviewed journal article

For CTA in the ER; “prospective studies were selected in which patients meeting specific chest pain and clinical criteria for evaluation with CTA were chosen to have the test.”

Seven studies (480 patients) were evaluated for CT diagnostic accuracy, and 2 studies (100 patients) for CTA in the ER. The TEC reported: “The available evidence is inadequate to determine whether CTA improves the net health outcome or is as beneficial as established alternatives for diagnosis of coronary artery stenosis or for evaluation of acute chest pain in the ER.”
The TEC criteria and results were as follows:
1. The technology must have final approval from the appropriate governmental bodies. (Met)
2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes. (Not met)
3. The technology must improve the net health outcome. (Not met)
4. The technology must be as beneficial as any established alternatives. (Not met)
5. The improvement must be attainable outside the investigational settings. (Not met)
They concluded: “CTA as a substitute for coronary angiography in the diagnosis of coronary artery stenosis does not meet the TEC criteria. CTA in the evaluation of acute chest pain in the emergency room also does not meet the TEC criteria.”

3. Internal technology assessments

Meta-Analyses

Hamon M, Biondi-Zoccai G, Malagutti P, et al. Diagnostic performance of multislice spiral computed tomography of coronary arteries as compared with conventional invasive coronary angiography. A meta-analysis. J Am Coll Cardiol 2006;48:1896 –1910.

In 2006, Hamon and colleagues reported the results of a meta-analysis "to define the current role of multislice spiral computed tomography (MSCT) for the diagnosis of coronary artery disease (CAD) using a meta-analytic process." The authors included 29 studies (2024 patients), published from 2002 to 2006, that evaluated the coronary arteries using both CTA (at least 16 slice) and conventional coronary angiography. Study inclusion criteria were: "1) it used MSCT as a diagnostic test for obstructive CAD, with >50% diameter stenosis selected as the cut-off criterion for significant CAD, using conventional invasive angiography as the reference standard; 2) it used the newest generation of MSCT (≥16 slices); and 3) it reported cases in absolute numbers of true positive (TP), false positive (FP), true negative (TN), and false negative (FN) results or presented sufficiently detailed data for deriving these figures." Exclusion criteria were studies performed: "1) only in patients after coronary artery bypass graft surgery; 2) after percutaneous coronary intervention for long-term stent patency assessment; 3) in a subset of patients with prior heart transplant; or 4) with fewer than 30 enrolled patients." Patient symptomatology was not specified. A random-effects model was used for the analysis.

The authors noted a considerable percentage of uninterpretable segments that were excluded from the analysis by the study investigators. Pooled sensitivity, specificity, positive and negative predictive values per-segment were 81%, 93%, 67.8% and 96.5%, respectively, and per patient were 96%, 74%, 83% and 94%, respectively.

The authors concluded: “Multislice spiral computed tomography has shortcomings difficult to overcome in daily practice and, at the more clinically relevant per-patient analysis, continues to have moderate specificity in patients with high prevalence of CAD. Studies evaluating the diagnostic performance of the newest generation of MSCT, including patients with low to moderate CAD prevalence, will be critical in establishing the clinical role of this emerging technology as an alternative to CA.”

Schuijf JD, Bax JJ, Shaw LJ, et al. Meta-analysis of comparative diagnostic performance of magnetic resonance imaging and multislice computed tomography for noninvasive coronary angiography. Am Heart J 2006;151:404- 11.

In 2006, Schuijf and colleagues reported the results of a meta-analysis “to clarify the current accuracy of both modalities in the detection of significant coronary artery lesions (compared to conventional angiography as the gold standard).” The authors included 24 studies (1300 patients), published from 2001 to 2005, that compared MSCT (4 to 16 slice) to invasive coronary angiography in patients with known or suspected CAD. Reports with insufficient data to calculate sensitivity and specificity were excluded. Meta-analysis model was not specified. Summary odds ratios were calculated using the “Comprehensive Meta Analysis” program. The authors reported pooled test parameters as follows: sensitivity 85%, specificity 95%, PPV 76% and NPV 97%. They concluded: “Meta-analysis of the available studies with MRI and MSCT for noninvasive coronary angiography indicates that MSCT has currently a significantly higher accuracy to detect or exclude significant coronary artery disease.”

Sun Z, Jiang W. Diagnostic value of multislice computed tomography angiography in coronary artery disease: A meta-analysis. European Journal of Radiology 2006;60:279–286.

In 2006, Sun and Jiang reported the results of a meta-analysis to determine “the diagnostic value of multislice CT (MSCT) angiography in the detection of coronary artery disease (CAD) when compared to conventional coronary angiography.” The authors included 47 studies (3149 patients), published from 2001 to 2006, that studied at least 4 slice CT. Study inclusion criteria were: “(a) patients undergoing both MSCT angiography and coronary angiography examinations; (b) studies included at least 10 patients; (c) assessment or comparison of MSCT angiography with coronary angiography was focused on the visualization of coronary arteries and detection or exclusion of coronary artery stenosis; (d) diagnostic value of MSCT angiography was addressed when compared to coronary angiography in terms of sensitivity, specificity, either segments-, vessels- or patients-based assessment.” Exclusion criteria, study types, patient symptomatology and setting were not specified. Model for analysis was not specified.

The authors reported pooled sensitivities and specificities for 4, 16 and 64 slice CT in the detection of CAD (76%, 93%; 82%, 95%; 92%, 94%; respectively). They concluded that: “MSCT angiography has potential diagnostic accuracy in the detection of CAD. Diagnostic performance of MSCT angiography has been significantly improved with the latest 64-slice CT, with resultant high qualitative and quantitative diagnostic accuracy. 16-slice CT was limited in spatial resolution which makes it difficult to perform quantitative assessment of coronary artery stenoses.”

Systematic Reviews

Janne d’Othee B, Siebert U, Cury R, et al. A systematic review on diagnostic accuracy of CT-based detection of significant coronary artery disease. European Journal of Radiology 2007, in Press.

In 2007, Janne d'Othee and colleagues reported the results of a systematic review to estimate sensitivity and specificity of various imaging modalities. Studies were included if they "used contrast-enhanced CT as a diagnostic test, evaluated native coronary arteries, used catheter-based coronary angiography (CCA) as a reference standard independently of CT findings, reported raw data (i.e., numbers that allowed recalculation of 2×2 contingency tables), and were published in peer reviewed journals." Coronary artery bypass graft and coronary stent studies were excluded. Catheter based coronary angiography was the reference standard.

Forty-one studies (2515 patients) were analyzed. A random effects model was used to calculate summary estimates. The authors reported: "Analysis of all coronary segments yielded a sensitivity of 95% (80%, 89%, 86%, 98% for electron beam CT, 4/8-slice, 16-slice and 64-slice MDCT, respectively) for a specificity of 85% (77%, 84%, 95%, 91%)." They noted: "In conclusion, recent advances in CT technology have resulted in an increase in the proportion of coronary segments assessable by CT and in improved diagnostic accuracy from EBCT to 4/8, 16, and 64-slice MDCT. The latter improvement is best demonstrated by the all-segment analysis. With current 64 slice scanners, diagnostic accuracy of CE-CCT is high on a per segment basis. Per patient however, this accuracy may be lower in patients with multi-vessel disease, which may limit the clinical utility of CT in populations at high risk for CAD. The utility of CT in patients with intermediate risk for CAD remains to be established."

Stein PD, Beemath A, Kayali F, et al. Multidetector computed tomography for the diagnosis of coronary artery disease: a systematic review. American Journal of Medicine 2006;119: 203-216.

In 2006, Stein and colleagues reported the results of a meta-analysis "to determine the sensitivity and specificity of contrast-enhanced multidetector computed tomography (CT) for the detection of coronary artery disease." The authors included 33 studies (1606 patients), published from 2001 to 2005, that compared MSCT (4 to 16 slice and 1 study on 64 slice) with invasive coronary angiography. Studies were included if they reported type of machines, data on sensitivity and specificity and patient selection criteria. Abstracts, in vitro studies, series with $\leq$ 10 patients were among those excluded. Meta-analysis model was not specified. Average sensitivity and specificity were calculated from pooled data.

The authors reported: “Average sensitivity for patient-based detection of significant (>50% or ≥50%) stenosis was 61 of 64 (95%) with 4-slice CT, 276 of 292 (95%) with 16-slice CT, and 47 of 47 (100%) with 64-slice CT. Average specificity was 84% for 4-slice CT, 84% for 16-slice CT, and 100% for 64-slice CT.” They concluded: “Multidetector CT has the potential to be used as a screening test in appropriate patients. Contrast-enhanced 16-slice CT seems to be reasonably sensitive and specific for the detection of significant coronary artery disease but has shortcomings. Preliminary data with 64-slice CT suggest that it is more sensitive and specific.”

16 Slice MSCT

Garcia MJ, Lessick J, Hoffmann MHK, CATSCAN investigators. Accuracy of 16-Row Multidetector Computed Tomography for the Assessment of Coronary Artery Stenosis. JAMA 2006;296:403-411.

In 2006, Garcia and colleagues reported the results of a case series of 238 patients “to determine the diagnostic accuracy of 16-row MDCT for the detection of obstructive coronary disease.” Included patients were between 30 and 70 years of age who were referred for clinically indicated nonemergency coronary angiography, for evaluation of chest pain, and for intermediate or high probability of disease. Exclusion criteria included prior bypass surgery, arrhythmias, pacemakers/defibrillators, renal insufficiency and contrast allergy. MDCT was performed using 16 row scanners and was done prior to invasive angiography. Invasive angiography was the reference standard. Of the 238 patients, 187 underwent 16 row MDCT with contrast and β blocker drugs. Forty-five percent of patients were classified as intermediate risk for CAD and 55% as high risk, according to the ACC/AHA guidelines (Gibbons et al., 2002). Invasive angiography was the reference standard. Mean age was 60 years. Men comprised 68% of the study population. Of the 1629 segments, 29% were uninterpretable.

The authors reported: After censoring all nonevaluable segments as positive, the sensitivity for detecting more than 50% luminal stenoses was 89%; specificity, 65%; positive predictive value, 13%; and negative predictive value, 99%. In a patient-based analysis, the sensitivity for detecting patients with at least 1 positive segment was 98%; specificity, 54%; positive predictive value, 50%; and negative predictive value, 99%.”

The authors concluded: “The results of this study indicate that MDCT coronary angiography performed with 16-row scanners is limited by a high number of nonevaluable cases and a high false-positive rate. Thus, its routine implementation in clinical practice is not justified. Nevertheless, given its high sensitivity and negative predictive value, 16-row MDCT may be useful in excluding coronary disease in selected patients in whom a false-positive or inconclusive stress test result is suspected.” There was no follow-up on health outcomes.

Hoffmann MHK, Shi H, Schmitz BL, et al. Noninvasive coronary angiography with multislice computed tomography. JAMA 2005;293:2471-2478.

In 2005, Hoffmann and colleagues reported the results of a case series of 103 patients “to assess the accuracy and robustness of MSCT vs the criterion standard of invasive coronary angiography for detection of obstructive coronary artery disease.” All patients had suspected CAD, were in sinus rhythm, were able to hold their breath for 25 seconds, and had been referred for invasive coronary angiography prior to inclusion in the study. Exclusion criteria included prior revascularization, renal insufficiency and contrast allergy. Scans were performed using a 16 detector MSCT with contrast and β blocker drugs. Pretest probability for CAD was assessed according to ACC/AHA guidelines (Gibbons et al., 2002). Invasive coronary angiography was the reference standard. Mean age was 62 years. Men comprised 69% of the study population. For CAD, 2% were determined to have low probability; 63% at intermediate probability; and d 35% at high probability.

The authors reported: “Compared with invasive coronary angiography for detection of significant lesions (>50% stenosis), segment-based sensitivity, specificity, and positive and negative predictive values of MSCT were 95%, 98%, 87%, and 99%, respectively.” These estimates excluded 27% of the study patients who had “only partial coronary tree coverage available.” Of the 1384 segments, 88 (6.4%) were uninterpretable. Sensitivity, specificity, and positive and negative predictive values per patient were 97%, 87%, 90%, 95%, respectively. The authors concluded: “Multislice computed tomography provides high accuracy for noninvasive detection of suspected obstructive coronary artery disease. This promising technology has potential to complement diagnostic invasive coronary angiography in routine clinical care.” There was no follow-up on health outcomes.

Kuettner A, Beck T, Drosch T, et al. Diagnostic accuracy of noninvasive coronary imaging using 16-detector slice spiral computed tomography with 188 ms temporal resolution. J Am Coll Cardiol 2005;45:123–127.

In 2005, Kuettner and colleagues reported the results of a case series of 72 patients "to evaluate the diagnostic accuracy of 16-multi-detector spiral computed tomography (MDCT) with 188 ms temporal resolution." All patients were scheduled for invasive angiography and also underwent MDCT imaging. Exclusion criteria include arrhythmias, renal insufficiency and contrast allergy. Scans were performed using 16 detector MDCT with contrast and β blocker drugs. Pretest risk was not specified. Invasive angiography was the reference standard. Mean age was 64 years. Men comprised 63% of the study population.

The authors reported: "Sensitivity, specificity, and positive and negative predictive values for the whole study group were as follows: 82%, 98%, 87%, and 97%, respectively. The correct clinical diagnosis of presence or absence of significant CAD was obtained in 65 of 72 (90%) patients." Of the 936 segments, 62 (6.6%) were uninterpretable. Per patient estimates were not reported. The authors noted: "In conclusion, noninvasive MDCT imaging is becoming more and more accurate. However, further improvements of spatial and temporal resolution are still required to challenge diagnostic invasive coronary angiography." There was no follow -up on health outcomes.

Mollet NR, Cademartiri1 F, Mieghem CV, et al. Adjunctive value of CT coronary angiography in the diagnostic work-up of patients with typical angina pectoris. European Heart Journal 2007;28:1872–1878.

In 2007, Mollet and colleagues reported the results of a consecutive series of 62 patients “to determine the adjunctive value of CT coronary angiography (CTCA) in the diagnostic work-up of patients with typical angina pectoris.” Patients included had typical angina, sinus heart rhythm and were able to hold their breaths for at least 20 seconds. Exclusion criteria included arrhythmias, renal insufficiency and contrast allergy. Scans were performed using 16 slice CT with contrast and β blocker drugs. Pre-test probability was high (81%). Invasive angiography was the reference standard. Mean age was 59 years. Men comprised 73% of the study population.

The authors reported sensitivity, specificity, PPV, NPV of 100%, 87%, 96%, 100%, respectively, per patient. They concluded: “Non-invasive CTCA is a potentially useful tool, in the diagnostic work-up of patients with typical angina pectoris, both to detect and to exclude significant CAD.” They also noted: “We have studied a relatively small number of patients who are at high risk of having significant CAD and excluded a significant number of patients because of logistic inability to perform CTCA before the conventional angiogram.” Health outcomes were not reported.

64 Slice MSCT

Meijboom WB, Mollet NR, Van Mieghem CA, et al. 64-slice computed tomography coronary angiography in patients with non-ST elevation acute coronary syndrome. Heart 2007 (online);doi:10.1136/hrt.2006.112771.

In 2007, Meijboom and colleagues reported the results of a non-consecutive case series of 104 patients to study “the diagnostic performance of 64-slice CT coronary angiography in patients with non-ST elevation acute coronary syndrome.” Patients presented with either unstable angina or non-ST elevation myocardial infarction. Exclusion criteria included atrial fibrillation, renal insufficiency and contrast allergy. Scans were performed using 64 slice CT with contrast and β blocker drugs. Pre-test risk was either high (68%) or low with positive or inconclusive exercise tests or high suspicion of CAD (32%). Invasive angiography was the reference standard. Mean age was about 59 years. Men comprised 72% of the study population.

The authors reported sensitivity, specificity, PPV, NPV of 100%, 75%%, 96%, 100%, respectively, per patient. Of the 1525 segments evaluated, 243 (15.9%) were not visualized and excluded. They concluded: “64-slice CT angiography has a high sensitivity to detect significant coronary stenoses and is reliable to exclude the presence of significant coronary artery disease in patients who present with a non-ST elevation acute coronary syndrome. The role of CT coronary angiography in these patients, particular in the lower risk group, needs to be further evaluated.” Health outcomes were not reported.

Francone M, Napoli A, Carbone I, et al. Noninvasive imaging of the coronary arteries using a 64-row multidetector CT scanner: initial clinical experience and radiation dose concerns. Radiol med 2007;112:31–46.

In 2007, Francone and colleagues reported the results of a case series of 114 patients to evaluate 64 detector CT. Of the 114 patients, 23 patients had MDCT to evaluate the coronary arteries for typical or atypical chest pain, 37 for evaluation of stent patency, 40 for patency of bypass grafts, 3 for inconclusive myocardial perfusion scintigraphy, and 11 for inconclusive stress echocardiography. Exclusion criteria included arrhythmia, kidney failure and contrast allergy. Scans were performed using 64 detector MDCT with contrast and β blocker drugs. Pretest risk was not reported. No reference standard was specified. Mean age was 63 years. Findings were not separately presented for the group of patients with chest pain. Test parameters and assessable segments were not reported.

The authors concluded: “In our initial clinical experience, the use of 64-MDCT has provided very promising results. Although the technique needs to be validated with systematic comparisons with clinical, laboratory and coronarographic data, the latest generation of 64-MDCT scanners offers new possibilities for clinical management of patients with coronary artery disease. The increase in spatial and temporal resolution translates into improved diagnostic image quality with respect to previous generations of multidetector devices. Thus, 64-MDCT is a noninvasive technique capable of identifying patients requiring interventional or surgical procedures such as selective coronarography with primary angioplasty or stent placement, or surgical revascularisation with bypass grafts. The use of suitable systems for the automatic control of radiation exposure seems nonetheless indispensable in order to limit patient dose, which given the current state of affairs is the main limitation to the clinical use of the technique.”

Ehara M, Surmely J, Kawai M, et al. Diagnostic accuracy of 64-slice computed tomography for detecting angiographically significant coronary artery stenosis in an unselected consecutive patient population. Circ J 2006;70:564–571.

In 2006, Ehara and colleagues reported the results of a case series of 69 patients "to investigate the accuracy of 64-slice MSCT (64 MSCT) in daily practice, without any patient selection." Nineteen patients with suspected CAD, 50 patients with proven CAD were enrolled. Exclusion criteria included arrhythmias, renal insufficiency and contrast allergy. Scans were performed using a 64 slice MSCT machine with contrast and β blocker drugs as needed. Pretest risk was not specified. Reference standard was invasive angiography. Mean age was 67 years. Men comprised 75% of the study population.

The authors reported: "Compared with ICAG (invasive coronary angiography) the sensitivity of CTA to diagnose significant stenosis was 90%, specificity 94%, positive predictive value (PPV) 89% and negative predictive value (NPV) 95%. With regard to 58 stented lesions, the sensitivity, specificity, PPV and NPV were 93%, 96%, 87% and 98%, respectively. On the patient-based analysis, the sensitivity, specificity, PPV and NPV of CTA to detect CAD were 98%, 86%, 98% and 86%, respectively." Of the 966 segments, 82 (8%) were uninterpretable. The authors concluded: "Sixty-four-MSCT has a high accuracy for the detection of significant CAD in an unselected patient population and therefore can be considered as a valuable noninvasive technique." No health outcomes were reported.

Ropers D, Rixe J, Anders K, et al. Usefulness of multidetector row spiral computed tomography with 64- X 0.6-mm collimation and 330-ms rotation for the noninvasive detection of significant coronary artery stenoses. Am J Cardiol 2006;97:343–348.

In 2006, Ropers and colleagues reported the results of a case series of 84 patients to analyze “the accuracy of 64-slice MDCT coronary angiography for the detection of significant coronary artery stenoses compared with quantitative coronary angiography.” All patients enrolled in the study had been referred for invasive angiography due to suspected CAD. Exclusion criteria included acute coronary syndromes, arrhythmias, and contrast allergy. Scans were performed using 64 slice MDCT with contrast and β blocker drugs. Pretest risk was not specified. Invasive angiography was the reference standard. Mean age was 58 years. Men comprised 62% of the study population. The authors reported: “After exclusion of unevaluable coronary segments (4%), multidetector computed tomography demonstrated a sensitivity of 93%, a specificity of 97%, and a negative predictive value of 100% in a per-segment analysis. In a per-artery analysis, 15 of 336 arteries (4%) were unevaluable. Sensitivity and specificity in evaluable arteries were 95% and 93%, respectively. In a per-patient analysis (81 of 84 patients included), sensitivity and specificity were 96% and 91%, respectively.”

Other Nonspecified CTA

Budoff MJ, Gopal A, Gul KM, et al. Prevalence of obstructive coronary artery disease in an outpatient cardiac CT angiography environment. International Journal of Cardiology 2007; In Press.

In 2007, Budoff and colleagues reported the results of a descriptive study of 493 patients “to determine the prevalence of significant obstructive disease and non-diagnostic studies using coronary computed tomographic angiography (CTA) in an outpatient environment, to establish if CTA could help avoid unnecessary diagnostic cardiac catheterizations.” All patients that received CTA “over one year with an indication that could warrant a cardiac catheterization to establish the presence or absence of coronary artery disease (CAD).” Exclusion criteria included prior myocardial infarction, revascularization and congenital heart diseases. “Referred patients generally had an intermediate pre-test probability of obstructive disease (20–80%).” Specific pretest risks were not noted. Scans were performed using an electron beam scanner with unspecified detectors. Reference standard was not used for all patients. Mean age was 58 years. Men comprised 68% of the population. The authors reported: "Of the 493 index cases evaluated, 157 (32%) cases were reported to be normal, 204 patients were classified as having nonobstructive disease (41%), 93 patients were defined to have obstructive CAD (19%), and 39 cases were inconclusive (8%).” Sensitivity, specificity and predictive values were not reported. In this study, there was no comparison test. There was no follow-up on health outcomes and patients who received invasive angiography subsequently.

Dual Source CT

Heuschmid M, Burgstahler C, Reimann A, et al. Usefulness of noninvasive cardiac imaging using dual-source computed tomography in an unselected population with high prevalence of coronary artery disease. Am J Cardiol 2007;100:587–592.

In 2007, Heuschmid and colleagues reported the results of a case series of 51 patients “to evaluate the diagnostic accuracy of new DSCT in unselected patients with a high prevalence of CAD, irregular heart rate, and extensive calcific deposits.” All patients were scheduled for invasive angiography due to CAD. Exclusion criteria were unstable angina, renal insufficiency, allergy to contrast. Scans were performed using DSCT with contrast. Pretest risk was not specified. Invasive angiography was the reference standard. Mean age was 64 years. Men comprised 73% of the study population.

The authors reported: Based on a coronary segment model, sensitivity was 96%, specificity 87%, positive predictive value 61%, and negative predictive value 99% for the detection of significant lesions (>50% diameter stenosis).” Of the 632 segments that were not stented, 117 (18.5%) were uninterpretable. They concluded: “our initial data indicate that DSCT allows a high accuracy to exclude relevant coronary stenosis in unselected patients with a high prevalence of CAD and a relevant number with heart rhythm irregularities. However, overestimation of stenosis, especially in cases of calcifications, is still a limitation.” There was no follow-up on health outcomes.

Weustink AC, Meijboom WB, Moller NR, et al. Reliable high-speed coronary computed tomography in symptomatic patients. J Am Coll Cardiol 2007;50:786–794.

In 2007, Weustink and colleagues reported the results of a case series of 100 patients with chest pain “to prospectively evaluate the diagnostic performance of the high-speed dual-source computed tomography scanner (DSCT), with an increased temporal resolution (83 ms), for the detection of significant coronary lesions (≥50% lumen diameter reduction) in a clinically wide range of patients.” All patients were symptomatic with “atypical angina, typical angina, and unstable coronary artery disease (unstable angina or non–ST segment elevation myocardial infarction) scheduled for conventional coronary angiography (CCA).” Patients with arrhythmias, past percutaneous coronary intervention, or bypass surgery, and allergy to contrast were excluded. Scans were performed using DSCT with contrast with nitroglycerin medication. Pretest risk was not specified. Invasive angiography was the reference standard. Mean age was 61 years. Men comprised 79% of the study population.

The authors reported: “Sensitivity, specificity, and positive and negative predictive values of DSCT coronary angiography for the detection of significant lesions on a segment-by-segment analysis were 95% (95% confidence interval [CI] 90 to 97), 95% (95% CI 93 to 96), 75% (95% CI 69 to 80), 99% (95% CI 98 to 99), respectively, and on a patient-based analysis 99% (95% CI 92 to 100), 87% (95% CI 65 to 97), 96% (95% CI 89 to 99), and 95% (95% CI 74 to 100), respectively.” Image quality was poor in 14% of the coronary segments. They concluded: “Dual source computed tomography scanner coronary angiography demonstrated a high diagnostic accuracy for the detection or exclusion of significant stenoses in patients with various heart rates without exclusion of unevaluable segments. These results indicate that the technique may now be tested in a cohort with a low-to-intermediate pretest probability of coronary artery disease or in patients with nonanginal chest pain to establish the role of DSCT coronary angiography in the management of patients with suspected coronary artery disease.”

Scheffel H, Alkadhi H, Plass A, et al. Accuracy of dual-source CT coronary angiography: first experience in a high pre-test probability population without heart rate control. Eur Radiol 2006;16:2739–2747.

In 2006, Scheffel and colleagues reported the results of a case series of 30 patients “to assess the diagnostic accuracy of dual source computed tomography (DSCT) for evaluation of coronary artery disease (CAD) in a population with extensive coronary calcifications without heart rate control.” Thirty patients who had invasive coronary angiography were included in the study. DSCT was performed within 30 days of catheterization. Exclusion criteria included previous stent or bypass surgery, renal insufficiency and contrast allergy. Scans were performed using DSCT with contrast and nitrate drugs. Based on a clinical score developed by Morise and colleagues (Morise et al., 1997), all patients were determined to have high pre-test probability of CAD. Invasive coronary angiography was the reference standard. Mean age was 63 years. Men comprised 80% of the study population.

The authors reported: “Overall sensitivity, specificity, positive and negative predictive value for evaluating CAD were 96.4, 97.5, 85.7, and 99.4%, respectively.” Of the 420 coronary segments, 6 (1.4%) were uninterpretable. They concluded: “First experience indicates that DSCT coronary angiography provides high diagnostic accuracy for assessment of CAD in a high pre-test probability population with extensive coronary calcifications and without heart rate control. Further studies are needed to confirm our results in appropriate clinical settings with larger patient populations.”

CTA of the coronary arteries in the ER Compared to Invasive Coronary Angiography

Goldstein JA, Gallagher MJ, O’Neil WW, et al. A randomized controlled trial of multi-slice coronary computed tomography for evaluation of acute chest pain. J Am Coll Cardiol 2007;49:863–871.

In 2007, Goldstein and colleagues reported the results of a randomized controlled trial “to compare the safety, diagnostic efficacy, and efficiency of multi-slice computed tomography (MSCT) with standard diagnostic evaluation of low-risk acute chest pain patients.” Inclusion criteria were chest pain or angina equivalent symptoms compatible with ischemia during the past 12 hours, age ≥25 years; and a prediction of a low risk of infarction and/or complications. Estimation of risk was done using a previously published clinical decision rule (Reilly et al., 2002). Exclusion criteria included known coronary artery disease, electrocardiograms diagnostic of cardiac ischemia and/or infarction, elevated serum biomarkers, contraindication to iodinated contrast and/or beta-blocking drugs, and atrial fibrillation or markedly irregular rhythm. Outcomes included safety, diagnostic efficacy, time and cost of care. Of the 197 patients, 99 were randomly assigned to receive MSCT (64 slice) with contrast and β blocker drugs and 98 to standard care (nuclear stress testing). Mean age was about 50 years. Men comprised about 50% of the study population. Almost all patients (196/197) were determined to be at very low risk using the Goldman Reilly criteria.

The authors reported no deaths, no myocardial infarctions, or other major adverse events in either group at 6 months. There was a significant difference in the proportion of patients discharged home from the ER (88% in the MSCT group versus 97% in the SOC group; p-value=0.03). The number of cardiac catheterizations at 6 months were not significantly different (12% in the MSCT group versus 7% in the SOC group; p-value=0.24). The MSCT scans were considered inadequate in 24.1% (24/99) of the patients and these patients then underwent nuclear stress testing. The authors concluded: “Multi-slice computed tomographic coronary angiography can definitively establish or exclude coronary disease as the cause of chest pain. However, inability to determine the physiological significance of intermediate severity coronary lesions and cases with inadequate image quality are present limitations.”

Olivetti L, Mazza G, Volpi D, et al. Multislice CT in emergency room management of patients with chest pain and medium-low probability of acute coronary syndrome. Radiol med 2006);111:1054–1063.

In 2006, Olivetti and colleagues reported the results of a case series of 31 patients “to evaluate the diagnostic accuracy of a 16-channel computed tomography (CT) scanner with dedicated software in a group of patients with chest pain and medium to low risk of ACS.” Inclusion criteria was “chest pain that was defined as medium to low probability of ACS” (absence of ischemic ECG ST changes and negative serum biomarkers). Exclusion criteria included previous revascularization, elevated heart rate, arrhythmias, various cardiac devices, and adverse reactions to contrast material. Scans were performed using 16 channel MDCT with contrast and β blocker drugs. Invasive angiography was the reference standard. Mean age was 59 years. Men comprised 61% of the study population. All patients received CT imaging and coronary angiography. The authors reported: “sensitivity of 65%, a specificity of 98.8%, a positive predictive value (PPV) of 81.2%, a negative predictive value (NPV) of 97.3% and an accuracy of 96.4%.” Of the 469 segments visualized, 383 (81.7%) were considered assessable. Image quality was considered “poor” in 19.8% of the segments (76/383). The authors concluded: “Due to its high NPV, this technique can rule out significant stenoses or coronary occlusions provided that image quality is excellent. In patients with a medium to low coronary risk, MSCT is a more accurate indicator of the need for coronary angiography than is exercise stress testing, which is less expensive but has lower predictive values.”

4. MEDCAC

A meeting of the Medicare Coverage Advisory Committee was held on May 18, 2006 to publicly discuss non-invasive diagnostic imaging compared with coronary artery angiography in the diagnosis of coronary artery disease. Information about the meeting including the technology assessment commissioned by CMS, panel questions and voting results and transcript are available on our website at http://www.cms.hhs.gov/mcd/viewmcac.asp?where=index&mid=34. The technology assessment is reviewed in a previous section of this document.

The panel voted on six questions using a 1 - 5 scale with 1 representing a “very unconfident” vote and 5 representing a “very confident” vote. The scores of the nine voting panel members were recorded and the average was calculated.

The first question asked whether the evidence was sufficient to conclude that CTA is accurate to diagnose obstructive coronary artery lesions. The panel voted on this question for both 16-slice CT and 64-slice CT. The average voting member score was 3.44 and 3.56 respectively. On the 1 to 5 scale, a score of 3 represents a vote of “unsure”. The second question asked whether the evidence was sufficient to conclude that CTA could accurately determine the anatomic location of obstructive coronary artery lesions. For the 16-slice technology, the average score of the voting members was 4.0 and for 64-slice the average score was 4.11. On the scale, a score of 4 represents a vote of “somewhat confident”. Question three asked whether the evidence was sufficient to conclude that CTA could accurately detect the relevant morphology (size, shape, ulceration, etc.) of obstructive coronary artery lesions. The average voting members score was 3.33 for both the 16-slice and 64-slice technologies.

Regarding the panel’s confidence regarding whether CTA can replace coronary catheterization to determine treatment of CAD (question four), the average score for 16-slice was 3.22 and for 64-slice was 3.44. When used in addition to catheterization, question five asked whether CTA provided an incremental benefit. The first part of the question asked about the incremental benefit of CTA when performed before catheterization for 16 and 64-slice. The average panel vote was 2.75 and 3.13 respectively. The second part of the question related to incremental benefit when performed after catheterization. For 16-slice, the average panel vote was 2.56 and for 64-slice was 3.00. A score of 2 on the scale represents a vote of “somewhat unconfident”.

In question six, the panel vote was 2.44 (16-slice) and 2.67 (64-slice) as to whether the test characteristics were generalizable to the Medicare beneficiary population. On the second part of question six, the panel voted 2.67 (16-slice) and 3.00 (64-slice) as to whether the diagnostic or treatment strategies using CTA for CAD would provide a net health benefit to Medicare beneficiaries when compared to invasive imaging.

5. Evidence-based guidelines

Budoff MJ, Achenbach S, Blumenthal RS, et al. Assessment of coronary artery disease by cardiac computed tomography: A scientific statement from the American Heart Association Committee on Cardiovascular Imaging and Intervention, Council on Cardiovascular Radiology and Intervention, and Committee on Cardiac Imaging, Council on Clinical Cardiology. Circulation 2006;114;1761-1791.

In 2006, Budoff and colleagues published a joint society statement based on evidence and opinion on the use of CTA in patients with CAD. The authors reported: “The studies that have evaluated the accuracy of EBCT and MDCT “coronary angiography” for the assessment of coronary artery stenoses have been relatively small (up to 149 individuals). They recruited somewhat selected patients (eg, excluding patients with acute coronary syndromes or atrial fibrillation), and all studies have been validated against invasive coronary angiography as a gold standard. No outcomes-based analyses that made further clinical management dependent on the EBCT or MDCT result have been published. However, all studies have convincingly demonstrated a very high negative predictive value of CT coronary angiography (see Table 8). Thus, a “normal” CT coronary angiogram allows the clinician to rule out the presence of hemodynamically relevant coronary artery stenoses with a high degree of reliability. When considering whether to refer a patient for EBCT or MDCT, clinicians must weigh the relative advantages of other testing methods such as exercise testing or stress imaging. The choice of testing will be determined by both local expertise in a given hospital as well as by the patient’s specific clinical history. Functional information demonstrating the physiological significance of coronary lesions is still paramount for decision-making related to revascularization. In a clinical context, the high negative predictive value may be useful for obviating the need for invasive coronary angiography in patients whose symptoms or abnormal stress test results make it necessary to rule out the presence of coronary artery stenoses. Especially if symptoms, age, and gender suggest a low to intermediate probability of hemodynamically relevant stenoses, ruling out hemodynamically relevant stenoses by CT coronary angiography may be clinically useful and may help avoid invasive angiography. CT coronary angiography is reasonable for the assessment of obstructive disease in symptomatic patients (Class IIa, Level of Evidence: B). Use of CT angiography in asymptomatic persons as a screening test for atherosclerosis (noncalcific plaque) is not recommended (Class III, Level of Evidence: C).”

6. Professional Society Position Statements

Hendel RC, Patel MR, Kramer CM, Poon M. ACCF/ACR/SCCT/SCMR/ASNC/NASCI/SCAI/SIR 2006 appropriateness criteria for cardiac computed tomography and cardiac magnetic resonance imaging: a report of the American College of Cardiology Foundation/American College of Radiology, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, American Society of Nuclear Cardiology, North American Society for Cardiac Imaging, Society for Cardiovascular Angiography and Interventions, and Society of Interventional Radiology. J Am Coll Cardiol 2006;48:1475–1497.

In 2006, a multispecialty group published appropriateness criteria for CT that were developed using a process that "blends scientific evidence and practice experience by engaging a Technical Panel in a modified Delphi exercise." The group produced an appropriateness score for 39 indications. Specific indications that were considered appropriate (score 7 to 9 out of 9) include:

Detection of CAD: Symptomatic—Acute Chest Pain, Intermediate pre-test probability of CAD, No ECG changes and serial enzymes negative - A(7);
Detection of CAD With Prior Test Results—Evaluation of Chest Pain Syndrome, Uninterpretable or equivocal stress test (exercise, perfusion, or stress echo) - A(8).

Pre-test probability of CAD was determined by "a modification of a literature review recommended by the American College of Cardiology/American Heart Association (ACC/AHA) 2002 Guideline Update for Exercise Testing and ACC/AHA 2002 Guideline Update for Management of Patients with Chronic Stable Angina" (references).

Jacobs JE, Boxt LM, Desjardins B, et al. ACR practice guideline for the performance and interpretation of cardiac computed tomography (CT). J Am Coll Radiol 2006;3:677-685.

In 2006, Jacobs and colleagues reported practice guidelines from the American College of Radiology “to help practitioners provide appropriate radiologic care for patients.” Recommendations were presented on indications for cardiac CT, physician qualifications and responsibilities. Cardiac CT is indicated for evaluation of “atherosclerosis,” and eleven other indications. As noted by ACR: “Each practice guideline and technical standard, representing a policy statement by the College, has undergone a thorough consensus process in which it has been subjected to extensive review, requiring the approval of the Commission on Quality and Safety as well as the ACR Board of Chancellors, the ACR Council Steering Committee, and the ACR Council.” The evidence basis for the guidelines is not reviewed to support the recommendations in this article.

7. Public Comments

CMS received 127 comments during the initial 30-day public comment period. Nine were from medical professional societies and other professional organizations and of the remaining 118, 18 of those included references and citations to clinical evidence.

Comments from Professional Societies and Organizations

CMS received comments from the following; America’s Health Insurance Plans, American College of Cardiology and American College of Radiology (combined comment), American Heart Association (AHA), American Society of Nuclear Cardiology, Cardiology Advocacy Alliance, Medical Imaging Technology Alliance, Society of Atherosclerosis Imaging and Prevention, Society of Cardiovascular Computed Tomography and Society of Interventional Radiology.

Eight commenters recommended that CMS not proceed with an NCD and allow Medicare contractors to determine coverage through the Local Coverage Determinations (LCDs) that many contractors already have in place and that provide coverage for CTA. Seven of the comments specifically cited and recommended the indications for CTA as outlined in the AHA scientific statement and multi-society consensus document that establishes appropriateness criteria. Five comments referred to “health outcomes” as an inappropriate threshold for measuring non-invasive diagnostic tests as such a measure does not take into account the value of ruling out disease, patient quality of life or impact on patient management. Four comments urge CMS to recognize the high negative predictive value of CTA and that a negative CTA test can avoid additional and invasive testing. Two comments highlight the concern for potential patient harms related to radiation exposure with CTA. Two comments recognize the potential of CTA as a diagnostic tool but believe there is need for additional data to fill in gaps in evidence. These two comments support an NCD that incorporates coverage with evidence development (prospective data collection and analysis plan). One comment recommended that CMS address the value of calcium scoring through the NCD, one comment recommended that CMS refrain from including specific CT equipment standards in a policy and one comment supported utilizing existing physician and lab credentialing programs.

Comments with Evidence

Comments with evidence are public comments in which the commenter included references to publicly available information. There were 18 of these comments that were not previously summarized in the above section for professional societies and organizations.

Clinical Uses
Commenters pointed to the AHA scientific statement and multi-society consensus document in support of clinical indications for national coverage (those documents and indications are discussed in earlier sections of this memorandum). Commenters provided additional information for varying clinical indications. The ability to identify and characterize plaque composition was cited by three commenters as being suggested in the literature to improve patient outcomes and predict future cardiac events. One commenter suggested that the literature demonstrates that CTA can diagnose CAD where stress perfusion studies cannot as in one study that shows ½ of the patients with normal perfusion scans were diagnosed as having CAD on the basis of CTA. A few commenters specifically mentioned the literature in support of CTA in symptomatic patients with an equivocal stress test with one commenter referencing that if CTA were used, angiography could be avoided in 60% of patients with an equivocal or abnormal stress test.

One commenter stated that studies have shown that CTA when used in the emergency department for patients presenting with chest pain has a 97% negative predictive value and a 52% positive predictive value. Another commenter stated that the negative predictive value is highest when used in a population for other predictive instruments (e.g. Framingham risk score) are also used. A second commenter emphasized this point by pointing to a study that had clinical outcomes as an endpoint and showed that test performance in a low prevalence population may differ from test performance in a high prevalence population.

Commenters state that studies show that use of CTA in the emergency department yields shorter hospital visits and saves time by diagnosing a patient earlier and for patients with negative test results, discharging them faster. Commenters used this information to support cost savings when compared to invasive angiography and radionuclide testing. A commenter referenced one study and registry data that estimated a 37% reduction in the use of radionuclide testing when CTA was used.

Radiation Concerns
Referencing the study that showed lesser test performance in a low prevalence population, the commenter stated that 24% of CTA results in the study were considered inadequate and those patients had to go on to additional diagnostic testing. The commenter states that in such cases where CTA does not replace other tests the patient is exposed to additional radiation through further testing. However, one commenter stated that based on a CTA registry, data showed that CTA is replacing invasive angiography and perfusion and more patients are being sent to CTA. Another commenter shares the concern and points to the risk associated with contrast medium according to a study that showed a 4:1000 incidence of acute renal damage. This commenter puts additional emphasis on this finding stating that there would be additional concerns in the Medicare population due to age and co-morbidities. In referencing the available assessments of CTA, one commenter expressed concern that the long term outcomes of radiation exposure from CTA have not been studied. One commenter suggested that newer scanner technology can reduce the radiation exposure, potentially making is lower than that of invasive angiography.

Technology/Equipment

One commenter states that a recent study suggests the value of 16-detector CT. Two commenters recommend not including any equipment standards in national policy because of the rapid evolvement of the technology.

Coverage with Evidence Development
Commenters referenced studies that are currently underway and recommend that CMS implement a policy to support such CTA trials to insure that they will continue. Commenters were concerned that there is a lack of evidence related to improved patient outcomes in the use of CTA to triage patients with acute chest pain or to diagnose CAD. One commenter stated the need for CMS to support randomized controlled studies comparing clinically important outcomes and potential harms with standard of care in order to develop a rigorous evidence base.

Comments without Evidence

Commenters cited language CMS used on the tracking sheet and stated that the agency had pre-judged the value of CTA. Additionally, commenters believed that “improved health outcome” is an inappropriate measure for noninvasive diagnostic tests rather, sensitivity and sensitivity and the impact on clinical decision making should be the measures. Commenters also pointed out that “rapid adoption” of a technology as stated on the tracking sheet does not equate to inappropriate use of the technology. Some commenters believed that it is too early to adopt national policy as studies and registries are ongoing.

The majority of commenters recommended that CMS not adopt an NCD and allow coverage to remain at the discretion of each local Medicare contractor. Most Medicare contractors have consistent local coverage determinations (LCDs) allowing coverage of CTA. Commenters stated that LCDs can better react to changes in technology which is particularly important with CT. However, if an NCD is adopted then commenters believed that the policy should be absent technological requirements for scanners due to rapid changes in equipment technology and that scanner mechanics do not serve as reliable proxies for quality images.

Commenters provided indications for which CTA should be covered including patients: presenting with chest pain; with an abnormal nuclear scan, equivocal perfusion study or equivocal stress test; with suspected congenital anomalies; with idiopathic cardiomyopathies; with suspected vulnerable plaque; at high risk of adverse events with catheterization; pre-operative and post-operative with cardiac surgery to assess graft patency; pre-operative of elective surgeries to rule out CAD. Other comments stated that CTA should not be used for various indications including in acute coronary events, patients with a high likelihood of CAD based on risk assessment and patients with previous angiographic diagnosis of CAD.

Commenters stated or refuted concerns related to radiation exposure. Concerns included the overall concern of radiation exposure for this test and the possibility of increased exposure through repeat testing. Others stated that CTA would replace other radioactive tests and that exposure is equivalent to a nuclear scan so the patient is subject to the same total exposure. Commenters also said that radiation exposure was less of a risk than the adverse events related to catheterization and that exposure is less of a concern in the elderly population since induced cancer is not a factor.

Cost was an issue addressed by some commenters. Most stated that because CTA is a noninvasive test that it is less costly than catheterization, also, that CTA reduces the hospital length of stay due to immediate diagnosis and can avoid additional testing. Other commenters expressed concern that the potential for self-referrals, abuse and over utilization could increase costs. Concern was also raised over the lack of training of certain medical specialties to appropriately interpret the scans.

In addition, some commenters supported Medicare coverage that would foster the technology and encourage additional studies that add evidence to the Medicare population. Commenters further suggested that existing registries be used as a mechanism of data collection while others supported prospective studies and randomized controlled trials as a requirement of Medicare coverage.

VIII. CMS Analysis

National coverage determinations (NCDs) are determinations by the Secretary with respect to whether or not a particular item or service is covered nationally under title XVIII of the Social Security Act § 1869(f)(1)(B). In order to be covered by Medicare, an item or service must fall within one or more benefit categories contained within Part A or Part B, and must not be otherwise excluded from coverage. Moreover, with limited exceptions, the expenses incurred for items or services must be "reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member." § 1862(a)(1)(A).

This analysis of the evidence focused on the following questions:

- Is the evidence sufficient to conclude that cardiac CTA has the ability to diagnosis or exclude coronary artery disease as well as invasive coronary angiography?
- Is the evidence sufficient to conclude that coronary CTA reduces the need for invasive coronary angiography?
- Is the evidence sufficient to conclude that the use of coronary CTA improves health outcomes for patients with acute chest pain who present in the emergency room or other settings?

Is the evidence sufficient to conclude that cardiac CTA has the ability to diagnosis or exclude coronary artery disease as well as invasive coronary angiography?

To evaluate this question on appropriateness, the test characteristics (sensitivity and specificity) and performance (positive and negative predictive values) of coronary CTA compared to invasive angiography, need to be considered. In general, sensitivity of a specific test is the proportion (percent) of people with the disease who have a positive test for the disease. Specificity is the proportion of people without the disease who have a negative test. Positive predictive value refers to the proportion of people with positive tests that actually have the disease as confirmed by the gold standard reference test (ability of coronary CTA to diagnose CAD compared to invasive angiography). Negative predictive value refers to the proportion of people with negative tests that actually do not have the disease as confirmed by the gold standard (ability of coronary CTA to rule out CAD compared to invasive angiography). Predictive values are determined by the sensitivity and specificity of the test and the prevalence of the disease.

Numerous studies have evaluated these parameters. Several technology assessments, meta-analyses and reviews have been published on coronary CTA in recent years. The BCBS TEC performed and published 2 technology assessments on coronary CTA (2005, 2006). The first evaluated CTA for evaluation of the coronary arteries, in general, while the latter focused on 32 or higher slice CT and use of coronary CTA in the emergency room. Both assessments found that coronary CTA did not meet TEC criteria. Three meta-analyses (Hamon, Schuijf, Sun) and 2 systematic reviews (Janne d'Othee, Stein) have been published and reported pooled test parameters (Table 1). Of the additional 11 published articles that we reviewed, 8 reported test parameters (Table 2).

Overall the reported sensitivity, specificity and predictive values are generally above 80-90%. However, these estimates have limitations in applicability and generalizability due to patient selection and potential bias. Although most studies did not report pretest risk, almost all patients enrolled in the reviewed studies were likely at relatively high risk for CAD, since these patients were already on the schedule for invasive coronary angiography (selected patient population). In general, test sensitivity and specificity will be higher when calculated in patients with more severe disease. The sensitivity and specificity estimates for coronary CTA based on high risk patients are not directly applicable to other patients at low or intermediate risk. Estimates calculated from data on low or intermediate risk patients have not been reported but most likely would be lower given the reduced severity of disease (spectrum bias[1]). These estimates, particularly for intermediate risk patients, are arguably more important since the role of coronary CTA appears to be more supported in these patients to avoid invasive angiography. The decision for invasive angiography is clinically variable for these patients; whereas, in high risk patients, invasive testing and interventions are likely to be recommended. Bias may also have been introduced if the interpretation of the CTA images were influenced by the results of the invasive angiography or other clinical data at the time of reading (unblinded). These issues are reflected in a 1999 report on design related bias in studies of diagnostic tests by Lijmer and colleagues, who noted: "The optimal design for assessing the accuracy of a diagnostic test is considered to be a prospective blind comparison of the test and the reference test in a consecutive series of patients from a relevant clinical population. A relevant clinical population is a group of patients covering the spectrum of disease that is likely to be encountered in the current for future use of the test."

The reported sensitivities and specificities also appear to vary somewhat, according to number of slices with a general trend that suggested the 64 slice machines had the best test estimates. This is consistent with the general consensus that 64 slice MSCT produces better images than the other variants.

Similar to sensitivity and specificity, the reported positive and negative predictive values of coronary CTA based on high risk patients are not directly applicable to low or intermediate risk patients because the prevalence of disease is different. The predictive values would very likely be lower if calculated using data from low or intermediate risk patients since these subpopulations have lower prevalence of CAD. If sensitivity and specificity were also to fall based on risk, then the reduction in predictive values would be more precipitous. Since parameters for low and intermediate risk populations have not been specifically reported and estimates from higher risk populations are not generalizable, the test characteristics and performance for these populations have not been adequately determined. The ability of coronary CTA to diagnose or exclude CAD for the majority of patients is unclear with the current evidence base.

Also problematic is the percentage of uninterpretable segments or uninterruptible images that have been reported (range from 4-29%), since these patients would likely then undergo invasive angiography. In a systematic review, Stein and colleagues (1996) reported: “One limitation has consistently been that a substantial number of coronary artery segments could not be evaluated for stenosis because of insufficient image quality.”

The AHA scientific statement noted that the reported high negative predictive values of coronary CTA may be “clinically useful” especially for patients with “low or intermediate probability of hemodynamically relevant stenoses” (Budoff et al., 2006). However, this statement appears to be based more on clinical opinion than evidence from research studies. As noted above, robust estimates of NPV have not been reported for these patients. This is reflected in the AHA classification given to coronary CTA for suspected CAD [Class IIa (conditions for which there is conflicting evidence, a divergence of opinion, or both about the usefulness/ efficacy of a procedure or treatment: weight of evidence/opinion is in favor of usefulness/efficacy.), Level of Evidence: B).[2]

For these reasons, the evidence is insufficient to conclude that cardiac CTA has the ability to diagnosis or exclude coronary artery disease as well as invasive coronary angiography. Thus, the evidence is inadequate to conclude that cardiac computed tomographic angiography (CTA) is reasonable and necessary under section 1861(a)(1)(A) for the diagnosis of coronary artery disease (CAD) Some preliminary evidence from case series on relatively high risk patients have been reported but not for the patients of most interest, the ones with intermediate risk of CAD. Additional research to determine test characteristics and performance is needed for these patients. This conclusion is consistent with the AHRQ / Duke EPC technology assessment, BCBS TEC assessments, meta-analysis by Hamon (MSCT has “shortcomings difficult to overcome in daily practice”) and Schuijf (“limited information is currently available on the accuracy of MSCT in low and intermediate prevalence populations”), and the systematic review by Janne d’Othee (“utility of CT in patients with intermediate risk for CAD remains to be established”).

While a clinically relevant population has not been fully studied, the published studies have shown promise for a technology that may have potential as a noninvasive approach for the diagnosis of CAD. With such potential, CMS believes additional research to develop the needed evidence on patient outcomes should be supported and that cardiac CTA for patients who are at intermediate risk of CAD be covered with coverage with evidence development (CED) under 1862(a)(1)(E).

Is the evidence sufficient to conclude that coronary CTA reduces the need for invasive coronary angiography?

One of the suggested benefits of coronary CTA is the reduction or avoidance of invasive angiography. However, none of the studies that evaluated diagnostic test performance were designed to generate evidence on reduction or avoidance of invasive angiography, since almost all patients were at relatively high risk and were already scheduled to undergo invasive coronary angiography. These studies also did not follow-up on health outcomes. One randomized trial (Goldstein et al., 2007) provided information on low risk patients that received CTA compared to standard of care. At 6 months, there was no significant difference in the number of cumulative cardiac catheterizations (12% in the MSCT group compared to 7% in standard care; p-value=0.24). No study has been published on patients at intermediate risk. Low risk patients would likely not undergo invasive angiography, while high risk patients would undergo invasive angiography regardless, so the need for an alternative test in these populations is reduced. There is insufficient evidence to conclude under 1862(a)(1)(A) that coronary CTA reduces the need for invasive angiography.

The AHA scientific statement noted a similar finding: “No outcomes-based analyses that made further clinical management dependent on the EBCT or MDCT result have been published” (Budoff et al., 2006). Under certain circumstances, MDCT may actually lead to increased non-invasive and invasive testing, if image quality is poor. Gershlich and colleagues from the British Cardiovascular Society (2006) reported: “Inappropriate use of MDCT as a first-line investigation at its current state of development is likely to result in an unwanted expansion in the need for non-invasive functional tests and even CA” (coronary angiography).

Is the evidence sufficient to conclude that the use of coronary CTA improves health outcomes for patients with acute chest pain who present in the emergency room?

In the 2006 assessment, the BCBS TEC reviewed 2 studies (White et al., 2005; Sato et al., 2005) on the use of coronary CTA for patients with chest pain in the emergency room. They stated that “these data do not demonstrate that CTA is an effective test for diagnosis of chest pain in the ER” (BCBS TEC, 2006). Although the settings were emergency rooms, neither study was designed to evaluate health outcomes. No follow-up of health outcomes were reported. We reviewed 2 additional studies: 1 randomized trial of 197 low risk patients (Goldstein et al., 2007) and 1 case series of 31 patients (Olivetti et al., 2006). As noted above, the trial by Goldstein and colleagues evaluated low risk patients who presented to the emergency room with chest pain using 64 slice MSCT. They reported no deaths or myocardial infarctions in either group at 6 months. There were no significant differences in rate of cumulative catheterizations, cumulative angioplasty and bypass surgery at 6 months. In the case series reported by Olivetti, there was no comparison group and health outcomes were not presented. The study by Goldstein did not support the use of coronary CTA in low risk patients. No study of health outcomes has been reported on intermediate risk patients. As noted earlier, health outcomes are more important than test characteristics, even for diagnostic tests. The value of a diagnostic test is in how the test results alter treatment and subsequently health outcomes. If the results of a test do not directly affect patient management, then it is unlikely to influence outcomes.

Thus, there is insufficient evidence to conclude that the use of coronary CTA improves health outcomes for patients with acute chest pain who present in the emergency room. Thus, the evidence is inadequate to conclude that cardiac computed tomographic angiography (CTA) is reasonable and necessary under section 1861(a)(1)(A) for patients who present with acute chest pain in the emergency room. This is consistent with the BCBS TEC assessments. Additional research on health outcomes is needed. The uncertainty of how coronary CTA fits into the currently recommended clinical pathways (AHA/ACC and ACP guidelines) was reflected in the AHA scientific statements as follows: “When considering whether to refer a patient for EBCT or MDCT, clinicians must weigh the relative advantages of other testing methods such as exercise testing or stress imaging. The choice of testing will be determined by both local expertise in a given hospital as well as by the patient’s specific clinical history. Functional information demonstrating the physiological significance of coronary lesions is still paramount for decision-making related to revascularization.”

Screening for CAD with Coronary CTA in Asymptomatic Individuals

From an epidemiologic standpoint, screening refers to the identification or detection of unrecognized, asymptomatic disease. Screening is important for conditions that cause significant morbidity and mortality when appropriate tests and treatments that improve health outcomes when provided at an earlier stage in the course of the disease are available. The use of coronary CTA for CAD screening has been suggested for asymptomatic (without chest pain syndrome) individuals. However, no randomized trials have been conducted and published on this use of CTA. No health outcomes have been studied for these patients. The criteria for an appropriate screening test have not been met. A number of technology assessments have been negative (BCBS TEC, HTA TEC). The AHA guidelines (Budoff et al., 2006) for coronary artery calcified plaque noted: “It is not recommended to use CACP measure in asymptomatic persons to establish the presence of obstructive disease for subsequent revascularization (Class III, Level of Evidence: C).” The ACC/AHA ranked detection of CAD with CTA as inappropriate for low and moderate risk patients and uncertain for high risk patients (Hendel, 2006). Thus screening for CAD with coronary CTA is not recommended in asymptomatic individuals.

Congress has not established a screening benefit for cardiac CTA for the diagnosis of CAD; thus the use of cardiac CTA to screen asymptomatic patients for CAD is noncovered.

Technology

There has been rapid advancement of the CTA technology from the initial 4 slice machines to the currently favored 64 slice scanners. Studies have been conducted using all these variants. As noted in various studies, the sensitivity and specificity appear to be higher with 64 slice MSCT. In addition, many have reported that the 64 slice MSCT produces considerably better quality images compared to the others. It also appears that this is a general consensus of the professional community and industry that 64 slice MSCT is the preferred choice for coronary CTA. With demonstrated technological improvements and general consensus, we have determined that coronary CTA should be performed with 32 slice or better CT machines. Another technology (dual source CT) has been developed but the number of reports (3 with a total of 181 patients) are small and the machines are not yet widely available.

Safety

The primary safety concerns are the exposure to considerable amounts of radiation, the use of β blocker medications and contrast. While we have not specifically focused on safety of coronary CTA, cumulative health outcomes are directly affected by the safety of any test and therefore influence the reasonable and necessary determination.

For a radiation risk reference point, the FDA stated (available at http://www.fda.gov/cdrh/ct/risks.html and in the Appendix C): “In the field of radiation protection, it is commonly assumed that the risk for adverse health effects from cancer is proportional to the amount of radiation dose absorbed and the amount of dose depends on the type of x-ray examination. A CT examination with an effective dose of 10 millisieverts (abbreviated mSv; 1 mSv = 1 mGy in the case of x rays.) may be associated with an increase in the possibility of fatal cancer of approximately 1 chance in 2000. This increase in the possibility of a fatal cancer from radiation can be compared to the natural incidence of fatal cancer in the U.S. population, about 1 chance in 5. In other words, for any one person the risk of radiation-induced cancer is much smaller than the natural risk of cancer. Nevertheless, this small increase in radiation-associated cancer risk for an individual can become a public health concern if large numbers of the population undergo increased numbers of CT screening procedures of uncertain benefit.” For radiation dose, the noted: “The effective doses from diagnostic CT procedures are typically estimated to be in the range of 1 to 10 mSv. This range is not much less than the lowest doses of 5 to 20 mSv received by some of the Japanese survivors of the atomic bombs. These survivors, who are estimated to have experienced doses only slightly larger than those encountered in CT, have demonstrated a small but increased radiation-related excess relative risk for cancer mortality.”

The radiation exposure from coronary CTA has received particular attention in recent publications since it may be much higher.

Paul and Abada (2007) reported: “Radiation dose is becoming a major issue for contrast enhanced cardiac multislice CT (coronary CT angiography), since 64-slice CT shows promising results for coronary artery evaluation. The radiation dose delivered for coronary CT angiography using retrospective gating is necessarily high because only part of the total radiation delivered is used for the reconstruction of the image in the current, commonly practised retrospective mode. The “useful” radiation corresponds to a temporal window of one phase of the cardiac cycle (for example the mid-diastole). This temporal window is determined by the rotation time of the machine; its value is about half the rotation time for amonophasic reconstruction. On average, only 20% of the radiation burden is used to reconstruct one phase of the cardiac cycle. In daily practice, computed tomography dose index (CTDI) for coronary CT angiography may reach or pass 100 mGy, with a dose-length product (DLP) of up to 2,000 (100 mGy×20 cm) if the entire thorax is scanned without application of dose-sparing tools. Thus, the effective dose may be up to about 40 mSv in female patients (corresponding to a DLP of 2,000 mGy·cm), and there are associated breast radiation issues. Cardiac patients may be exposed to various sources of medical radiation (including nuclear studies and conventional angiography), with repeated examinations, making radiation exposure risks certain when cumulated radiation dose exceeds 200 mSv. Due to these high radiation levels, it seems essential to minimise the radiation dose associated with cardiac CT examinations. Radiologists should be increasingly careful about radiation dose levels and should attempt to use dose-saving algorithms whenever possible”

The AHA (Budoff et al., 2006) also noted the risk of radiation exposure: “For CT angiography, the higher radiation doses suggest the need for greater forethought when using these tests, and use of these higher radiation exposure tests in asymptomatic persons for screening purposes is not currently recommended.” Einstein and colleagues (2007) reported that their “simulation models suggest that use of 64-slice CTCA is associated with a nonnegligible LAR (lifetime attributable risk) of cancer” and that the risk is “considerably greater for women, younger patients, and for combined cardiac and aortic scans.” As with most tests and interventions, risks and adverse events should be considered when deciding to perform the test in question and discussed with each patient prior to undergoing the test.

CED and Future Research

In addition to section 1862(a)(1)(A), a second statutory provision may permit Medicare payment for items and services in some circumstances. That statute, section 1862(a)(1)(E), provides, in pertinent part, that:
(a) Notwithstanding any other provision of this title, no payment may be made under part A or part B for any expenses incurred for items or services—

. . .
(E) in the case of research conducted pursuant to section 1142, which is not reasonable and necessary to carry out the purposes of that section[.]
. . .
Section 1142 describes the authority of the Agency for Healthcare Research and Quality (AHRQ).

Under the authority of section 1862(a)(1)(E), CMS pay for items and services furnished in connection with certain medical research. Coverage is conditioned on care being delivered in a setting with a pre-specified data collection process and additional protections in place such as are present in some research studies. Under section 1142, research may be conducted on the outcomes, effectiveness, and appropriateness of health care services and procedures to identify the manner in which diseases, disorders, and other health conditions can be prevented, diagnosed, treated, and managed clinically. In addition, evaluations of the comparative effects, health and functional capacity; alternative services and procedures utilized in preventing, diagnosing, treating, and clinically managing diseases, disorders, and other health conditions may be conducted.

In rare instances, for some items or services, CMS may determine that the evidence is very preliminary and not reasonable and necessary for Medicare coverage under section 1862(a)(1)(A), but, if the following criteria are met, Coverage with Evidence Development (CED) might be appropriate:
a. The evidence includes assurance of basic safety;
b. The item or service has a high potential to provide significant benefit to Medicare beneficiaries; and
c. There are significant barriers to conducting clinical trials.
These research studies will be rigorously designed and include additional protections and safety measures for beneficiaries.

To qualify for reimbursement, such a study must be designed to produce evidence that could be used in a future national coverage decision that would focus on whether the item or service should be covered by Medicare under 1862(a)(1)(A). Payment for the items and services provided in the study will be restricted to the Medicare qualified patients involved as human subjects in the study.

We have found the evidence to be inadequate and determine that CTA for the diagnosis of CAD is not reasonable and necessary under 1862(a)(1)(A). There is some evidence to suggest that there is a health benefit when CTA is used for the diagnosis of CAD for the following clinical indications is reasonable and necessary when conducted under clinical study (CED (1862(a)(1)(E)):

- symptomatic patients with chronic stable angina at intermediate risk of CAD or;
- symptomatic patients with unstable angina at a low risk of short-term death and intermediate risk of CAD.

A clinical study seeking Medicare payment for CTA for the diagnosis of CAD for the above clinical indications provided to the beneficiary pursuant to CED must address one or more of the following questions:

- Does cardiac CTA have the ability to diagnose or exclude coronary artery disease as well as invasive coronary angiography?
- Does coronary CTA reduce the need for invasive coronary angiography?
- Does coronary CTA improve health outcomes for patients with acute chest pain who present in the emergency room or other setting?

CMS is requiring that the study meet the following standards:

- The principal purpose of the research study is to test whether the intervention potentially improves the participants' health outcomes;
- The research study is well-supported by available scientific and medical information or it is intended to clarify or establish the health outcomes of interventions already in common clinical use;
- The research study does not unjustifiably duplicate existing studies;
- The research study design is appropriate to answer the research question being asked in the trial;
- The research study is sponsored by an organization or individual capable of executing the proposed trial successfully;
- The research study is in compliance with Federal regulations concerning the protection of human subjects found at 45 CFR Part 46. If a study is FDA-regulated, it also must be in compliance with 21 CFR Parts 50 and 56;

- All aspects of the research study are conducted according to the appropriate standards of scientific integrity.
- The research study has a written protocol that clearly addresses, or incorporates by reference, the Medicare standards;
- The research study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals. Trials of all medical technologies measuring therapeutic outcomes as one of the objectives meet this standard only if the disease or condition being studied is life-threatening as defined in 21 CFR §312.18(a) and the patient has no other viable treatment options;
- The research study is registered on the ClinicalTrials.gov website by the principal sponsor/investigator prior to the enrollment of the first study subject;
- The research study protocol specifies the method and timing of public release of all prespecified outcomes to be measured including release of outcomes if outcomes are negative or study is terminated early. The results must be made public within 24 months of the end of data collection. If a report is planned to be published in a peer-reviewed journal, then that initial release may be an abstract that meets the requirements of the International Committee of Medical Journal Editors. However, a full report of the outcomes must be made public no later than three years after the end of data collection.
- The research study protocol must explicitly discuss subpopulations affected by the treatment under investigation, particularly traditionally underrepresented groups in clinical studies, how the inclusion and exclusion criteria affect enrollment of these populations, and a plan for the retention and reporting of said populations on the trial. If the inclusion and exclusion criteria are expected to have a negative effect on recruitment or retention of the underrepresented populations, the protocol must discuss why these criteria are necessary; and
- The research study protocol explicitly discusses how the results are or are not expected to be generalizable to the Medicare population to infer whether Medicare patients may benefit from the intervention. Separate discussions in the protocol may be necessary for populations eligible for Medicare due to age, disability or Medicaid eligibility.

We have consulted with AHRQ who has agreed that the study questions and requirements outlined above are consistent with Section 1142 of the Act.

The principal investigators of CTA clinical studies seeking Medicare payment should submit the following documentation to CMS and should expect to be notified when the CMS review is complete:

- Complete study protocol;
- Protocol summary;

- Statement that the above study standards are met;
- Statement that the study addresses at least one of the above questions related to CTA;
- Complete contact information (phone number, email address and mailing address); and
- Clinicaltrials.gov registration number.

The above information should be mailed to:

Steve E. Phurrough, MD, MPA
Director
Coverage and Analysis Group, CMS
Re: CTA
Mailstop C1-09-06
7500 Security Blvd.
Baltimore, MD 21244-1850

The AHRQ technology assessment performed by the Duke EPC provided some additional recommendations for future research, quoted as follows:

There are three primary types of evidence that could address the question of substitution of non-invasive for invasive imaging: a randomized trial, an observational study ("natural experiment"), or a decision model.

A randomized trial could take several forms and could use either surrogate or patient-related outcomes. For example, patients with suspected CAD could be randomized to a strategy of "usual diagnostic evaluation," including invasive angiography when indicated, or usual diagnostic evaluation plus option for non-invasive coronary imaging. Alternatively, the patients could be randomized between early invasive and early non-invasive coronary imaging. Outcomes could include hard events such as death or MI, as well as efficiency measures including resource consumption and costs.

A “natural experiment” observational study would examine apparently similar patients referred for alternative diagnostic strategies, including early invasive, early non-invasive coronary imaging, and stress imaging. The notion of a “natural experiment” assumes that there is an element of randomness in clinical practice that can be exploited analytically. If the use of a technology in the practice community has matured to the point where there is significant confounding with patient characteristics, even advanced statistical adjustment techniques may not suffice to uncover unconfounded outcomes.

A decision model would examine the most likely diagnostic strategies of interest along with predicted health outcomes and resource use. Since there is a high level of dependency of test performance and treatment benefit and harm on clinical context, such considerations would likely require separate models. Further, sensitivity analyses to identify effects on decision thresholds are a central part of such an exercise.

IX. Summary

Based on the evidence reviewed, CMS believes that coronary CTA for the diagnosis of CAD is not reasonable and necessary under 1861(a)(1)(A); however, the agency believes the evidence is promising for two clinical indications and that coverage with evidence development would be appropriate for these indications under section 1862(a)(1)(E), based on the specific standards outlined above.

Therefore, CMS proposes Medicare coverage of CTA for the diagnosis of CAD only when performed under a study pursuant to the CED standards and when performed using 32-slice CT technology or higher for:

- symptomatic patients with chronic stable angina at intermediate risk of CAD or;
- symptomatic patients with unstable angina at a low risk of short-term death and intermediate risk of CAD.

Cardiac CTA for the diagnosis of CAD in other patient populations is noncovered.

Coverage of cardiac CTA for uses other than the diagnosis of CAD is at local contractor discretion.

CMS does not believe that sufficient evidence is available to demonstrate that CTA improves health outcomes in the Medicare population with chest pain at high risk for CAD. This population will almost certainly need angiography regardless of the results of this test. The data are not available that demonstrates that physicians will change patient management in this population. The additional risks inherent in CTA—potential for renal failure as well as the significant radiation exposure—are not offset by any benefits.

We also do not believe that sufficient evidence exists to demonstrate that CTA improves health outcomes in the Medicare population with chest pain at low risk for CAD. Empirical evidence from Goldstein was not favorable in this population.

While the evidence is also limited on the benefits of CTA in the intermediate risk population, it is this population that may have the potential to have significant benefits that may outweigh the risks. The applicability of estimates of sensitivity and specificity are limited in this group. Based on professional consensus, the American Heart Association stated that the negative predictive value of CTA may be “clinically useful” in this group, and needs to be confirmed in a study.

---

[1] Ransohoff and Feinstein noted: “Unless an appropriately broad spectrum is chosen for the diseased and nondiseased patients who comprise the study population, the diagnostic test may receive falsely high values for its "rule-in" and "rule-out" performances.”

[2] Reproduced from Budoff et al., 2006:
Classification of Recommendations

- Class I: Conditions for which there is evidence, general agreement, or both that a given procedure or treatment is useful and effective.
- Class II: Conditions for which there is conflicting evidence, a divergence of opinion, or both about the usefulness/ efficacy of a procedure or treatment.
    - Class IIa: Weight of evidence/opinion is in favor of usefulness/efficacy.
    - Class IIb: Usefulness/efficacy is less well established by evidence/opinion.
- Class III: Conditions for which there is evidence, general agreement, or both that the procedure/treatment is not useful/ effective and in some cases may be harmful.

Level of Evidence

- Level of Evidence A: Data derived from multiple randomized clinical trials
- Level of Evidence B: Data derived from a single randomized trial or nonrandomized studies
- Level of Evidence C: Consensus opinion of experts

Appendix A. NCD Manual (100.03)

220.1 - Computerized Tomography
(Rev. 1, 10-03-03)
CIM 50-12

A. General
Diagnostic examinations of the head (head scans) and of other parts of the body (body scans) performed by computerized tomography (CT) scanners are covered if medical and scientific literature and opinion support the effective use of a scan for the condition, and the scan is: (1) reasonable and necessary for the individual patient; and (2) performed on a model of CT equipment that meets the criteria in C below.

The CT scans have become the primary diagnostic tool for many conditions and symptoms. CT scanning used as the primary diagnostic tool can be cost effective because it can eliminate the need for a series of other tests, is noninvasive and thus virtually eliminates complications, and does not require hospitalization.

B. Determining Whether a CT Scan Is Reasonable and Necessary Sufficient information must be provided with claims to differentiate CT scans from other radiology services and to make coverage determinations. Carefully review claims to insure that a scan is reasonable and necessary for the individual patient; i.e., the use must be found to be medically appropriate considering the patient's symptoms and preliminary diagnosis.

There is no general rule that requires other diagnostic tests to be tried before CT scanning is used. However, in an individual case the contractor's medical staff may determine that use of a CT scan as the initial diagnostic test was not reasonable and necessary because it was not supported by the patient's symptoms or complaints stated on the claim form; e.g., "periodic headaches."

Claims for CT scans are reviewed for evidence of abuse which might include the absence of reasonable indications for the scans, an excessive number of scans or unnecessarily expensive types of scans considering the facts in the particular cases.

C. Approved Models of CT Equipment

1. Criteria for Approval

In the absence of evidence to the contrary, the contractor may assume that a CT scan for which payment is requested has been performed on equipment that meets the following criteria:

a. The model must be known to the Food and Drug Administration, and

b. Must be in the full market release phase of development.

Should it be necessary to confirm that those criteria are met, ask the manufacturer to submit the information in C.2. If manufacturers inquire about obtaining Medicare approval for their equipment, inform them of the foregoing criteria.

2. Evidence of Approval

a. The letter sent by the Bureau of Radiological Health, Food and Drug Administration (FDA), to the manufacturer acknowledging the FDA's receipt of information on the specific CT scanner system model submitted as required under Public Law 90-602, "The Radiation Control for Health and Safety Act of 1968."

b. A letter signed by the chief executive officer or other officer acting in a similar capacity for the manufacturer which:

1. Furnishes the CT scanner system model number, all names that hospitals and physicians' offices may use to refer to the CT scanner system on claims, and the accession number assigned by FDA to the specific model;
2. Specifies whether the scanner performs head scans only, body scans only (i.e., scans of parts of the body other than the head), or head and body scans;
3. States that the company or corporation is satisfied with the results of the developmental stages that preceded the full market release phase of the equipment, that the equipment is in the full market release phase, and the date on which it was decided to put the product into the full market release phase.

D. Mobile CT Equipment

The CT scans performed on mobile units are subject to the same Medicare coverage requirements applicable to scans performed on stationary units, as well as certain health and safety requirements recommended by Health Resources and Services Administration (HRSA). As with scans performed on stationary units, the scans must be determined medically necessary for the individual patient. The scans must be performed on types of CT scanning equipment that have been approved for use as stationary units (see C above), and must be in compliance with applicable State laws and regulations for control of radiation.

1. Hospital Setting

The hospital must assume responsibility for the quality of the scan furnished to inpatients and outpatients and must assure that a radiologist or other qualified physician is in charge of the procedure. The radiologist or other physician (i.e., one who is with the mobile unit) who is responsible for the procedure must be approved by the hospital for similar privileges.

2. Ambulatory Setting
If mobile CT scan services are furnished at an ambulatory health care facility other than a hospital-based facility, e.g., a freestanding physician-directed clinic, the diagnostic procedure must be performed by or under the direct personal supervision of a radiologist or other qualified physician. In addition, the facility must maintain a record of the attending physician's order for a scan performed on a mobile unit.

3. Billing for Mobile CT Scans
Hospitals, hospital-associated radiologists, ambulatory health care facilities, and physician owner/operators of mobile units may bill for mobile scans as they would for scans performed on stationary equipment.

4. Claims Review
Evidence of compliance with applicable State laws and regulations for control of radiation should be requested from owners of mobile CT scan units upon receipt of the first claims. All mobile scan claims should be reviewed very carefully in accordance with instructions applicable to scans performed on fixed units, with particular emphasis on the medical necessity for scans performed in an ambulatory setting.

E. Multi-Planar Diagnostic Imaging (MPDI)
In usual computerized tomography (CT) scanning procedures, a series of transverse or axial images are reproduced. These transverse images are routinely translated into coronal and/or sagittal views. Multi-planar diagnostic imaging (MPDI) is a process which further translates the data produced by CT scanning by providing reconstructed oblique images which can contribute to diagnostic information. MPDI, also known as planar image reconstruction or reformatted imaging, is covered under Medicare when provided as a service to an entity performing a covered CT scan.

Appendix B: General Methodological Principles of Study Design

When making national coverage determinations, CMS evaluates relevant clinical evidence to determine whether or not the evidence is of sufficient quality to support a finding that an item or service falling within a benefit category is reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. The critical appraisal of the evidence enables us to determine whether: 1) the specific assessment questions can be answered conclusively; and 2) the intervention will improve health outcomes for patients. An improved health outcome is one of several considerations in determining whether an item or service is reasonable and necessary.

CMS normally divides the assessment of clinical evidence into three stages: 1) the quality of the individual studies; 2) the relevance of findings from individual studies to the Medicare population; and 3) overarching conclusions that can be drawn from the body of the evidence on the direction and magnitude of the intervention's risks and benefits.

The issues presented here represent a broad discussion of the issues we consider when reviewing clinical evidence. However, it should be noted that each coverage determination has unique methodological aspects.

1. Assessing Individual Studies

Methodologists have developed criteria to determine weaknesses and strengths of clinical research. Strength of evidence generally refers to: 1) the scientific validity underlying study findings regarding causal relationships between health care interventions and health outcomes; and 2) the reduction of bias. In general, some of the methodological attributes associated with stronger evidence include those listed below:

- Use of randomization (allocation of patients to either intervention or control group) in order to minimize bias.
- Use of contemporaneous control groups (rather than historical controls) in order to ensure comparability between the intervention and control groups.

- Prospective (rather than retrospective) studies to ensure a more thorough and systematical assessment of factors related to outcomes.
- Larger sample sizes in studies to help ensure adequate numbers of patients are enrolled to demonstrate both statistically significant as well as clinically significant outcomes that can be extrapolated to the Medicare population. Sample size should be large enough to make chance an unlikely explanation for what was found.
- Masking (blinding) to ensure patients and investigators do not know to which group patients were assigned (intervention or control). This is important especially in subjective outcomes, such as pain or quality of life, where enthusiasm and psychological factors may lead to an improved perceived outcome by either the patient or assessor.

Regardless of whether the design of a study is a randomized controlled trial, a non-randomized controlled trial, a cohort study or a case-control study, the primary criterion for methodological strength or quality is the extent to which differences between intervention and control groups can be attributed to the intervention studied. This is known as internal validity. Various types of bias can undermine internal validity. These include:

- Different characteristics between patients participating and those theoretically eligible for study but not participating (selection bias)
- Co-interventions or provision of care apart from the intervention under evaluation (confounding)
- Differential assessment of outcome (detection bias)
- Occurrence and reporting of patients who do not complete the study (attrition bias)

In principle, rankings of research design have been based on the ability of each study design category to minimize these biases. A randomized controlled trial minimizes systematic bias (in theory) by selecting a sample of participants from a particular population and allocating them randomly to the intervention and control groups. Thus, randomized controlled studies have been typically assigned the greatest strength, followed by non-randomized clinical trials and controlled observational studies. The following is a representative list of study designs (some of which have alternative names) ranked from most to least methodologically rigorous in their potential ability to minimize systematic bias:

- Randomized controlled trials
- Non-randomized controlled trials
- Prospective cohort studies
- Retrospective case control studies
- Cross-sectional studies

- Surveillance studies (e.g., using registries or surveys)
- Consecutive case series
- Single case reports

When there are merely associations but not causal relationships between a study's variables and outcomes, it is important not to draw causal inferences. Confounding refers to independent variables that systematically vary with the causal variable. This distorts measurement of the outcome of interest because its effect size is mixed with the effects of other extraneous factors. For observational, and in some cases randomized controlled trials, the method in which confounding factors are handled (either through stratification or appropriate statistical modeling) are of particular concern. For example, in order to interpret and generalize conclusions to our population of Medicare patients, it may be necessary for studies to match or stratify their intervention and control groups by patient age or co-morbidities.

Methodological strength is, therefore, a multidimensional concept that relates to the design, implementation and analysis of a clinical study. In addition, thorough documentation of the conduct of the research, particularly study's selection criteria, rate of attrition and process for data collection, is essential for CMS to adequately assess the evidence.

2. Generalizability of Clinical Evidence to the Medicare Population

The applicability of the results of a study to other populations, settings, treatment regimens, and outcomes assessed is known as external validity. Even well-designed and well-conducted trials may not supply the evidence needed if the results of a study are not applicable to the Medicare population. Evidence that provides accurate information about a population or setting not well represented in the Medicare program would be considered but would suffer from limited generalizability.

The extent to which the results of a trial are applicable to other circumstances is often a matter of judgment that depends on specific study characteristics, primarily the patient population studied (age, sex, severity of disease, and presence of co-morbidities) and the care setting (primary to tertiary level of care, as well as the experience and specialization of the care provider). Additional relevant variables are treatment regimens (dosage, timing, and route of administration), co-interventions or concomitant therapies, and type of outcome and length of follow-up.

The level of care and the experience of the providers in the study are other crucial elements in assessing a study's external validity. Trial participants in an academic medical center may receive more or different attention than is typically available in non-tertiary settings. For example, an investigator's lengthy and detailed explanations of the potential benefits of the intervention and/or the use of new equipment provided to the academic center by the study sponsor may raise doubts about the applicability of study findings to community practice.

Given the evidence available in the research literature, some degree of generalization about an intervention's potential benefits and harms is invariably required in making coverage decisions for the Medicare population. Conditions that assist us in making reasonable generalizations are biologic plausibility, similarities between the populations studied and Medicare patients (age, sex, ethnicity and clinical presentation), and similarities of the intervention studied to those that would be routinely available in community practice.

A study's selected outcomes are an important consideration in generalizing available clinical evidence to Medicare coverage determinations because one of the goals of our determination process is to assess health outcomes. We are interested in the results of changed patient management not just altered management. These outcomes include resultant risks and benefits such as increased or decreased morbidity and mortality. In order to make this determination, it is often necessary to evaluate whether the strength of the evidence is adequate to draw conclusions about the direction and magnitude of each individual outcome relevant to the intervention under study. In addition, it is important that an intervention's benefits are clinically significant and durable, rather than marginal or short-lived.

If key health outcomes have not been studied or the direction of clinical effect is inconclusive, we may also evaluate the strength and adequacy of indirect evidence linking intermediate or surrogate outcomes to our outcomes of interest.

3. Assessing the Relative Magnitude of Risks and Benefits

Generally, an intervention is not reasonable and necessary if its risks outweigh its benefits. Improved health outcomes are one of several considerations in determining whether an item or service is reasonable and necessary. For most determinations, CMS evaluates whether reported benefits translate into improved health outcomes. CMS places greater emphasis on health outcomes actually experienced by patients, such as quality of life, functional status, duration of disability, morbidity and mortality, and less emphasis on outcomes that patients do not directly experience, such as intermediate outcomes, surrogate outcomes, and laboratory or radiographic responses. The direction, magnitude, and consistency of the risks and benefits across studies are also important considerations. Based on the analysis of the strength of the evidence, CMS assesses the relative magnitude of an intervention or technology's benefits and risk of harm to Medicare beneficiaries.

Appendix C. Diagrams and Tables [PDF, 453KB]
Back to Top

Bibliography

Anderson JL, Adams CD, Antman EM, et al. ACC/AHA 2007 guidelines for the management of patients with unstable angina/non–ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines for the Management of Patients With Unstable Angina/Non–ST-Elevation Myocardial Infarction): developed in collaboration with the American College of Emergency Physicians, American College of Physicians, Society for Academic Emergency Medicine, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. J Am Coll Cardiol 2007;50:e1–157.

Blue Cross Blue Shield Technology Evaluation Center. Contrast-enhanced cardiac computed tomographic angiography in the diagnosis of coronary artery stenosis or for evaluation of acute chest pain. TEC Assessment Program, Volume 20, No. 4, May 2005.

Blue Cross Blue Shield Technology Evaluation Center. Contrast-enhanced cardiac computed tomographic angiography in the diagnosis of coronary artery stenosis or for evaluation of acute chest pain. TEC Assessment Program, Volume 21, No. 5, August 2006.

Budoff MJ, Achenbach S, Blumenthal RS, et al. Assessment of coronary artery disease by cardiac computed tomography: A scientific statement from the American Heart Association Committee on Cardiovascular Imaging and Intervention, Council on Cardiovascular Radiology and Intervention, and Committee on Cardiac Imaging, Council on Clinical Cardiology. Circulation 2006;114;1761-1791.

Budoff MJ, Gopal A, Gul KM, et al. Prevalence of obstructive coronary artery disease in an outpatient cardiac CT angiography environment. International Journal of Cardiology 2007; In Press.

DHHS Agency for Healthcare Research and Quality. Non-Invasive Imaging for Coronary Artery Disease. AHRQ 2006; available at: http://www.cms.hhs.gov/determinationprocess/downloads/id34TA.pdf.

Douglas P, Chen J, Gillam L, et al. Achieving quality in cardiovascular imaging: proceedings from the American College of Cardiology–Duke University Medical Center Think Tank on Quality in Cardiovascular Imaging. J Am Coll Cardiol 2006;48:2141–2151.

Ehara M, Surmely J, Kawai M, et al. Diagnostic accuracy of 64-slice computed tomography for detecting angiographically significant coronary artery stenosis in an unselected consecutive patient population. Circ J 2006;70:564–571

Einstein AJ, Henzlova MJ, Rajagopalan S. Estimating risk of cancer associated with radiation exposure from 64-slice computed tomography coronary angiography. JAMA 2007;298:317-323

Francone M, Napoli A, Carbone I, et al. Noninvasive imaging of the coronary arteries using a 64-row multidetector CT scanner: initial clinical experience and radiation dose concerns. Radiol med 2007;112:31–46

Garcia MJ, Lessick J, Hoffmann MHK, CATSCAN investigators. Accuracy of 16-Row Multidetector Computed Tomography for the Assessment of Coronary Artery Stenosis. JAMA 2006;296:403-411.

Gibbons RJ, Abrams J, Chatterjee K, et al. ACC/AHA 2002 guideline update for the management of patients with chronic stable angina: a report of the American College of Cardiology/ American Heart Association Task Force on Practice Guidelines (Committee to Update the 1999 Guidelines for the Management of Patients with Chronic Stable Angina). 2002. Available at www.acc.org/clinical/guidelines/stable/stable.pdf.

Gibbons RJ, Balady GJ, Bricker JT, et al. ACC/AHA 2002 guideline update for exercise testing: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Exercise Testing). 2002. American College of Cardiology Web site. Available at: www.acc.org/clinical/guidelines/exercise/dirIndex.htm.

Goldstein JA, Gallagher MJ, O'Neil WW, et al. A randomized controlled trial of multi-slice coronary computed tomography for evaluation of acute chest pain. J Am Coll Cardiol 2007;49:863–871.

Hamon M, Biondi-Zoccai G, Malagutti P, et al. Diagnostic performance of multislice spiral computed tomography of coronary arteries as compared with conventional invasive coronary angiography. A meta-analysis. J Am Coll Cardiol 2006;48:1896 –1910.

Waugh N, Black C, Walker S, et al. The effectiveness and cost-effectiveness of computed tomography screening for coronary artery disease: systematic review. Health Technol Assess 2006;10(39).

Hendel RC, Patel MR, Kramer CM, Poon M.
ACCF/ACR/SCCT/SCMR/ASNC/NASCI/SCAI/SIR 2006 appropriateness criteria for cardiac computed tomography and cardiac magnetic resonance imaging: a report of the American College of Cardiology Foundation/American College of Radiology, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, American Society of Nuclear Cardiology, North American Society for Cardiac Imaging, Society for Cardiovascular Angiography and Interventions, and Society of Interventional Radiology. J Am Coll Cardiol 2006;48:1475–1497.

Heuschmid M, Burgstahler C, Reimann A, et al. Usefulness of noninvasive cardiac imaging using dual-source computed tomography in an unselected population with high prevalence of coronary artery disease. Am J Cardiol 2007;100:587–592.

Hoffmann MHK, Shi H, Schmitz BL, et al. Noninvasive coronary angiography with multislice computed tomography. JAMA 2005;293:2471-2478.

Jacobs JE, Boxt LM, Desjardins D, et al. ACR practice guideline for the performance and interpretation of cardiac computed tomography (CT). J Am Coll Radiol 2006;3:677-685.

Janne d'Othee B, Siebert U, Cury R, et al. A systematic review on diagnostic accuracy of CT-based detection of significant coronary artery disease. European Journal of Radiology 2007, in Press.

Keevil JC, Cullen MW, Gangnon R, et al. Dyslipidemia: Data from National Health and Nutrition Examination Survey distributions in the United States for the diagnosis and treatment of implications of cardiac risk and low-density lipoprotein cholesterol. Circulation 2007;115:1363-1370.

Kramer CM, Budoff MJ, Fayad ZA, et al. ACCF/AHA clinical competence statement on vascular imaging with computed tomography and magnetic resonance: a report of the American College of Cardiology Foundation/American Heart Association/American College of Physicians Task Force on Clinical Competence and Training. J Am Coll Cardiol 2007;50:1097–114.

Kuettner A, Beck T, Drosch T, et al. Diagnostic accuracy of noninvasive coronary imaging using 16-detector slice spiral computed tomography with 188 ms temporal resolution. J Am Coll Cardiol 2005;45:123–127.

Lijmer JG, Mol BW, Heisterkamp S, et al. Empirical evidence of design-related bias in studies of diagnostic tests. JAMA 1999;282:1061-1066.

Meijboom WB, Mollet NR, Van Mieghem CA, et al. 64-slice computed tomography coronary angiography in patients with non-ST elevation acute coronary syndrome. Heart 2007 (online);doi:10.1136/hrt.2006.112771.

Mol BW, Lijmer JG, Evers JL, Bossuyt PM. Characteristics of good diagnostic studies. Semin Reprod Med 2003;21:17-25.

Mollet NR, Cademartiri1 F, Mieghem CV, et al. Adjunctive value of CT coronary angiography in the diagnostic work-up of patients with typical angina pectoris. European Heart Journal 2007;28:1872–1878.

Paul JF, Abada HT. Strategies for reduction of radiation dose in cardiac multislice CT. Eur Radiol 2007;17: 2028–2037.

Olivetti L, Mazza G, Volpi D, et al. Multislice CT in emergency room management of patients with chest pain and medium-low probability of acute coronary syndrome. Radiol med 2006);111:1054–1063.

Ransohoff DF, Feinstein AR. Problems of spectrum and bias in evaluating the efficacy of diagnostic tests. N Engl J Med 1978;299:926-930.

Ropers D, Rixe J, Anders K, et al. Usefulness of multidetector row spiral computed tomography with 64- X 0.6-mm collimation and 330-ms rotation for the noninvasive detection of significant coronary artery stenoses. Am J Cardiol 2006;97:343–348.

Scheffel H, Alkadhi H, Plass A, et al. Accuracy of dual-source CT coronary angiography: first experience in a high pre-test probability population without heart rate control. Eur Radiol 2006;16:2739–2747.

Schuijf JD, Bax JJ, Shaw LJ, et al. Meta-analysis of comparative diagnostic performance of magnetic resonance imaging and multislice computed tomography for noninvasive coronary angiography. Am Heart J 2006;151:404- 11.

Snow V, Barry P, Fihn ED, et al. Evaluation of primary care patients with chronic stable angina: Guidelines from the American College of Physicians. Ann Intern Med 2004;141:57-64.

Stein PD, Beemath A, Kayali F, et al. Multidetector computed tomography for the diagnosis of coronary artery disease: a systematic review. American Journal of Medicine 2006;119: 203-216.

Sun Z, Jiang W. Diagnostic value of multislice computed tomography angiography in coronary artery disease: A meta-analysis. European Journal of Radiology 2006;60:279–286.

Weustink AC, Meijboom WB, Moller NR, et al. Reliable high-speed coronary computed tomography in symptomatic patients. J Am Coll Cardiol 2007;50:786–794.

Wilson PWF, D'Agostino RB, Levy L, et al. Prediction of coronary heart disease using risk factor categories. Circulation 1998;97:1837-1847.

Back to Top